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(21) International Application Number: PCT/US00/08896 (22) International Filing Date: 3 April 2000 (03.04.00) (30) Priority Data: <table border="0"><tr><td>09/285,479</td><td>2 April 1999 (02.04.99)</td><td>US</td></tr><tr><td>09/466,396</td><td>17 December 1999 (17.12.99)</td><td>US</td></tr><tr><td>09/476,496</td><td>30 December 1999 (30.12.99)</td><td>US</td></tr><tr><td>09/480,884</td><td>10 January 2000 (10.01.00)</td><td>US</td></tr><tr><td>09/510,376</td><td>22 February 2000 (22.02.00)</td><td>US</td></tr></table> (71) Applicant (for all designated States except US): CORIXA CORPORATION [US/US]; Suite 200, 1124 Columbia Street, Seattle, WA 98104 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): WANG, Tongtong [US/US]; 8049 NE 28th Street, Medina, WA 98039 (US). FAN, Lijun [CN/US]; 14116 SE 46th Street, Bellevue, WA 98006 (US). (74) Agents: MAKI, David, J.; Seed Intellectual Property Law Group PLLC, Suite 6300, 701 Fifth Avenue, Seattle, WA 98104-7092 (US) et al.		09/285,479	2 April 1999 (02.04.99)	US	09/466,396	17 December 1999 (17.12.99)	US	09/476,496	30 December 1999 (30.12.99)	US	09/480,884	10 January 2000 (10.01.00)	US	09/510,376	22 February 2000 (22.02.00)	US	(81) Designated States: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PE, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>Without international search report and to be republished upon receipt of that report.</i>
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(54) Title: COMPOUNDS AND METHODS FOR THERAPY AND DIAGNOSIS OF LUNG CANCER																	
(57) Abstract <p>Compounds and methods for the treatment and diagnosis of lung cancer are provided. The inventive compounds include polypeptides containing at least a portion of a lung tumor protein. Vaccines and pharmaceutical compositions for immunotherapy of lung cancer comprising such polypeptides, or DNA molecules encoding such polypeptides, are also provided, together with DNA molecules for preparing the inventive polypeptides.</p>																	

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COMPOUNDS AND METHODS FOR THERAPY AND DIAGNOSIS OF LUNG CANCER

TECHNICAL FIELD

5 The present invention relates generally to therapy and diagnosis of cancer, such as lung cancer. The invention is more specifically related to polypeptides comprising at least a portion of a lung tumor protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for prevention and treatment of lung cancer, and for the
10 diagnosis and monitoring of such cancers.

BACKGROUND OF THE INVENTION

Lung cancer is the primary cause of cancer death among both men and women in the U.S., with an estimated 172,000 new cases being reported in 1994. The five-year survival rate among all lung cancer patients, regardless of the stage of disease
15 at diagnosis, is only 13%. This contrasts with a five-year survival rate of 46% among cases detected while the disease is still localized. However, only 16% of lung cancers are discovered before the disease has spread.

Early detection is difficult since clinical symptoms are often not seen until the disease has reached an advanced stage. Currently, diagnosis is aided by the
20 use of chest x-rays, analysis of the type of cells contained in sputum and fiberoptic examination of the bronchial passages. Treatment regimens are determined by the type and stage of the cancer, and include surgery, radiation therapy and/or chemotherapy. In spite of considerable research into therapies for the disease, lung cancer remains difficult to treat.

25 Accordingly, there remains a need in the art for improved vaccines, treatment methods and diagnostic techniques for lung cancer.

SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compositions and methods for the diagnosis and therapy of cancer, such as lung cancer. In one aspect, the present

invention provides polypeptides comprising at least a portion of a lung tumor protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises a sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253-337, 345, 347 and 349; (b) variants of a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253-337, 345, 347 and 349; and (c) complements of a sequence of (a) or (b). In specific embodiments, the polypeptides of the present invention comprise at least a portion of a tumor protein that includes an amino acid sequence selected from the group consisting of sequences recited in any one of SEQ ID NO: 152, 155, 156, 165, 166, 169, 170, 172, 174, 176, 226-252, 338-344 and 346, and variants thereof.

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a lung tumor protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, vaccines for prophylactic or therapeutic use are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and an immunostimulant.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a lung tumor protein; and (b) a physiologically acceptable carrier.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above, and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with an immunostimulant.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a lung tumor protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a lung tumor protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Determined T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4⁺ and/or CD8⁺ T cells determined from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a lung tumor protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be lung cancer.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the

sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a lung tumor protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a lung tumor protein; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

5

SEQUENCE IDENTIFIERS

- SEQ ID NO: 1 is the determined cDNA sequence for LST-S1-2
- SEQ ID NO: 2 is the determined cDNA sequence for LST-S1-28
- SEQ ID NO: 3 is the determined cDNA sequence for LST-S1-90
- 10 SEQ ID NO: 4 is the determined cDNA sequence for LST-S1-144
- SEQ ID NO: 5 is the determined cDNA sequence for LST-S1-133
- SEQ ID NO: 6 is the determined cDNA sequence for LST-S1-169
- SEQ ID NO: 7 is the determined cDNA sequence for LST-S2-6
- SEQ ID NO: 8 is the determined cDNA sequence for LST-S2-11
- 15 SEQ ID NO: 9 is the determined cDNA sequence for LST-S2-17
- SEQ ID NO: 10 is the determined cDNA sequence for LST-S2-25
- SEQ ID NO: 11 is the determined cDNA sequence for LST-S2-39
- SEQ ID NO: 12 is a first determined cDNA sequence for LST-S2-43
- SEQ ID NO: 13 is a second determined cDNA sequence for LST-S2-43
- 20 SEQ ID NO: 14 is the determined cDNA sequence for LST-S2-65
- SEQ ID NO: 15 is the determined cDNA sequence for LST-S2-68
- SEQ ID NO: 16 is the determined cDNA sequence for LST-S2-72
- SEQ ID NO: 17 is the determined cDNA sequence for LST-S2-74
- SEQ ID NO: 18 is the determined cDNA sequence for LST-S2-103
- 25 SEQ ID NO: 19 is the determined cDNA sequence for LST-S2-N1-1F
- SEQ ID NO: 20 is the determined cDNA sequence for LST-S2-N1-2A
- SEQ ID NO: 21 is the determined cDNA sequence for LST-S2-N1-4H
- SEQ ID NO: 22 is the determined cDNA sequence for LST-S2-N1-5A
- SEQ ID NO: 23 is the determined cDNA sequence for LST-S2-N1-6B
- 30 SEQ ID NO: 24 is the determined cDNA sequence for LST-S2-N1-7B
- SEQ ID NO: 25 is the determined cDNA sequence for LST-S2-N1-7H

- SEQ ID NO: 26 is the determined cDNA sequence for LST-S2-N1-8A
- SEQ ID NO: 27 is the determined cDNA sequence for LST-S2-N1-8D
- SEQ ID NO: 28 is the determined cDNA sequence for LST-S2-N1-9A
- SEQ ID NO: 29 is the determined cDNA sequence for LST-S2-N1-9E
- 5 SEQ ID NO: 30 is the determined cDNA sequence for LST-S2-N1-10A
- SEQ ID NO: 31 is the determined cDNA sequence for LST-S2-N1-10G
- SEQ ID NO: 32 is the determined cDNA sequence for LST-S2-N1-11A
- SEQ ID NO: 33 is the determined cDNA sequence for LST-S2-N1-12C
- SEQ ID NO: 34 is the determined cDNA sequence for LST-S2-N1-12E
- 10 SEQ ID NO: 35 is the determined cDNA sequence for LST-S2-B1-3D
- SEQ ID NO: 36 is the determined cDNA sequence for LST-S2-B1-6C
- SEQ ID NO: 37 is the determined cDNA sequence for LST-S2-B1-5D
- SEQ ID NO: 38 is the determined cDNA sequence for LST-S2-B1-5F
- SEQ ID NO: 39 is the determined cDNA sequence for LST-S2-B1-6G
- 15 SEQ ID NO: 40 is the determined cDNA sequence for LST-S2-B1-8A
- SEQ ID NO: 41 is the determined cDNA sequence for LST-S2-B1-8D
- SEQ ID NO: 42 is the determined cDNA sequence for LST-S2-B1-10A
- SEQ ID NO: 43 is the determined cDNA sequence for LST-S2-B1-9B
- SEQ ID NO: 44 is the determined cDNA sequence for LST-S2-B1-9F
- 20 SEQ ID NO: 45 is the determined cDNA sequence for LST-S2-B1-12D
- SEQ ID NO: 46 is the determined cDNA sequence for LST-S2-I2-2B
- SEQ ID NO: 47 is the determined cDNA sequence for LST-S2-I2-5F
- SEQ ID NO: 48 is the determined cDNA sequence for LST-S2-I2-6B
- SEQ ID NO: 49 is the determined cDNA sequence for LST-S2-I2-7F
- 25 SEQ ID NO: 50 is the determined cDNA sequence for LST-S2-I2-8G
- SEQ ID NO: 51 is the determined cDNA sequence for LST-S2-I2-9E
- SEQ ID NO: 52 is the determined cDNA sequence for LST-S2-I2-12B
- SEQ ID NO: 53 is the determined cDNA sequence for LST-S2-H2-2C
- SEQ ID NO: 54 is the determined cDNA sequence for LST-S2-H2-1G
- 30 SEQ ID NO: 55 is the determined cDNA sequence for LST-S2-H2-4G
- SEQ ID NO: 56 is the determined cDNA sequence for LST-S2-H2-3H

- SEQ ID NO: 57 is the determined cDNA sequence for LST-S2-H2-5G
- SEQ ID NO: 58 is the determined cDNA sequence for LST-S2-H2-9B
- SEQ ID NO: 59 is the determined cDNA sequence for LST-S2-H2-10H
- SEQ ID NO: 60 is the determined cDNA sequence for LST-S2-H2-12D
- 5 SEQ ID NO: 61 is the determined cDNA sequence for LST-S3-2
- SEQ ID NO: 62 is the determined cDNA sequence for LST-S3-4
- SEQ ID NO: 63 is the determined cDNA sequence for LST-S3-7
- SEQ ID NO: 64 is the determined cDNA sequence for LST-S3-8
- SEQ ID NO: 65 is the determined cDNA sequence for LST-S3-12
- 10 SEQ ID NO: 66 is the determined cDNA sequence for LST-S3-13
- SEQ ID NO: 67 is the determined cDNA sequence for LST-S3-14
- SEQ ID NO: 68 is the determined cDNA sequence for LST-S3-16
- SEQ ID NO: 69 is the determined cDNA sequence for LST-S3-21
- SEQ ID NO: 70 is the determined cDNA sequence for LST-S3-22
- 15 SEQ ID NO: 71 is the determined cDNA sequence for LST-S1-7
- SEQ ID NO: 72 is the determined cDNA sequence for LST-S1-A-1E
- SEQ ID NO: 73 is the determined cDNA sequence for LST-S1-A-1G
- SEQ ID NO: 74 is the determined cDNA sequence for LST-S1-A-3E
- SEQ ID NO: 75 is the determined cDNA sequence for LST-S1-A-4E
- 20 SEQ ID NO: 76 is the determined cDNA sequence for LST-S1-A-6D
- SEQ ID NO: 77 is the determined cDNA sequence for LST-S1-A-8D
- SEQ ID NO: 78 is the determined cDNA sequence for LST-S1-A-10A
- SEQ ID NO: 79 is the determined cDNA sequence for LST-S1-A-10C
- SEQ ID NO: 80 is the determined cDNA sequence for LST-S1-A-9D
- 25 SEQ ID NO: 81 is the determined cDNA sequence for LST-S1-A-10D
- SEQ ID NO: 82 is the determined cDNA sequence for LST-S1-A-9H
- SEQ ID NO: 83 is the determined cDNA sequence for LST-S1-A-11D
- SEQ ID NO: 84 is the determined cDNA sequence for LST-S1-A-12D
- SEQ ID NO: 85 is the determined cDNA sequence for LST-S1-A-11E
- 30 SEQ ID NO: 86 is the determined cDNA sequence for LST-S1-A-12E
- SEQ ID NO: 87 is the determined cDNA sequence for L513S (T3).

- SEQ ID NO: 88 is the determined cDNA sequence for L513S contig 1.
- SEQ ID NO: 89 is a first determined cDNA sequence for L514S.
- SEQ ID NO: 90 is a second determined cDNA sequence for L514S.
- SEQ ID NO: 91 is a first determined cDNA sequence for L516S.
- 5 SEQ ID NO: 92 is a second determined cDNA sequence for L516S.
- SEQ ID NO: 93 is the determined cDNA sequence for L517S.
- SEQ ID NO: 94 is the extended cDNA sequence for LST-S1-169 (also known as L519S).
- SEQ ID NO: 95 is a first determined cDNA sequence for L520S.
- 10 SEQ ID NO: 96 is a second determined cDNA sequence for L520S.
- SEQ ID NO: 97 is a first determined cDNA sequence for L521S.
- SEQ ID NO: 98 is a second determined cDNA sequence for L521S.
- SEQ ID NO: 99 is the determined cDNA sequence for L522S.
- SEQ ID NO: 100 is the determined cDNA sequence for L523S.
- 15 SEQ ID NO: 101 is the determined cDNA sequence for L524S.
- SEQ ID NO: 102 is the determined cDNA sequence for L525S.
- SEQ ID NO: 103 is the determined cDNA sequence for L526S.
- SEQ ID NO: 104 is the determined cDNA sequence for L527S.
- SEQ ID NO: 105 is the determined cDNA sequence for L528S.
- 20 SEQ ID NO: 106 is the determined cDNA sequence for L529S.
- SEQ ID NO: 107 is a first determined cDNA sequence for L530S.
- SEQ ID NO: 108 is a second determined cDNA sequence for L530S.
- SEQ ID NO: 109 is the determined full-length cDNA sequence for L531S short form.
- SEQ ID NO: 110 is the predicted amino acid sequence encoded by SEQ ID NO: 109.
- 25 SEQ ID NO: 111 is the determined full-length cDNA sequence for L531S long form.
- SEQ ID NO: 112 is the predicted amino acid sequence encoded by SEQ ID NO: 111.
- SEQ ID NO: 113 is the determined full-length cDNA sequence for L520S.
- SEQ ID NO: 114 is the predicted amino acid sequence encoded by SEQ ID NO: 113.
- SEQ ID NO: 115 is the determined cDNA sequence for contig 1.
- 30 SEQ ID NO: 116 is the determined cDNA sequence for contig 3.
- SEQ ID NO: 117 is the determined cDNA sequence for contig 4.

- SEQ ID NO: 118 is the determined cDNA sequence for contig 5.
- SEQ ID NO: 119 is the determined cDNA sequence for contig 7.
- SEQ ID NO: 120 is the determined cDNA sequence for contig 8.
- SEQ ID NO: 121 is the determined cDNA sequence for contig 9.
- 5 SEQ ID NO: 122 is the determined cDNA sequence for contig 10.
- SEQ ID NO: 123 is the determined cDNA sequence for contig 12.
- SEQ ID NO: 124 is the determined cDNA sequence for contig 11.
- SEQ ID NO: 125 is the determined cDNA sequence for contig 13.
- SEQ ID NO: 126 is the determined cDNA sequence for contig 15.
- 10 SEQ ID NO: 127 is the determined cDNA sequence for contig 16.
- SEQ ID NO: 128 is the determined cDNA sequence for contig 17.
- SEQ ID NO: 129 is the determined cDNA sequence for contig 19.
- SEQ ID NO: 130 is the determined cDNA sequence for contig 20.
- SEQ ID NO: 131 is the determined cDNA sequence for contig 22.
- 15 SEQ ID NO: 132 is the determined cDNA sequence for contig 24.
- SEQ ID NO: 133 is the determined cDNA sequence for contig 29.
- SEQ ID NO: 134 is the determined cDNA sequence for contig 31.
- SEQ ID NO: 135 is the determined cDNA sequence for contig 33.
- SEQ ID NO: 136 is the determined cDNA sequence for contig 38.
- 20 SEQ ID NO: 137 is the determined cDNA sequence for contig 39.
- SEQ ID NO: 138 is the determined cDNA sequence for contig 41.
- SEQ ID NO: 139 is the determined cDNA sequence for contig 43.
- SEQ ID NO: 140 is the determined cDNA sequence for contig 44.
- SEQ ID NO: 141 is the determined cDNA sequence for contig 45.
- 25 SEQ ID NO: 142 is the determined cDNA sequence for contig 47.
- SEQ ID NO: 143 is the determined cDNA sequence for contig 48.
- SEQ ID NO: 144 is the determined cDNA sequence for contig 49.
- SEQ ID NO: 145 is the determined cDNA sequence for contig 50.
- SEQ ID NO: 146 is the determined cDNA sequence for contig 53.
- 30 SEQ ID NO: 147 is the determined cDNA sequence for contig 54.
- SEQ ID NO: 148 is the determined cDNA sequence for contig 56.

- SEQ ID NO: 149 is the determined cDNA sequence for contig 57.
- SEQ ID NO: 150 is the determined cDNA sequence for contig 58.
- SEQ ID NO: 151 is the full-length cDNA sequence for L530S.
- SEQ ID NO: 152 is the amino acid sequence encoded by SEQ ID NO: 151.
- 5 SEQ ID NO: 153 is the full-length cDNA sequence of a first variant of L514S.
- SEQ ID NO: 154 is the full-length cDNA sequence of a second variant of L514S.
- SEQ ID NO: 155 is the amino acid sequence encoded by SEQ ID NO: 153.
- SEQ ID NO: 156 is the amino acid sequence encoded by SEQ ID NO: 154.
- SEQ ID NO: 157 is the determined cDNA sequence for contig 59.
- 10 SEQ ID NO: 158 is the full-length cDNA sequence for L763P (also referred to as contig 22).
- SEQ ID NO: 159 is the amino acid sequence encoded by SEQ ID NO: 158.
- SEQ ID NO: 160 is the full-length cDNA sequence for L762P (also referred to as contig 17).
- 15 SEQ ID NO: 161 is the amino acid sequence encoded by SEQ ID NO: 160.
- SEQ ID NO: 162 is the determined cDNA sequence for L515S.
- SEQ ID NO: 163 is the full-length cDNA sequence of a first variant of L524S.
- SEQ ID NO: 164 is the full-length cDNA sequence of a second variant of L524S.
- SEQ ID NO: 165 is the amino acid sequence encoded by SEQ ID NO: 163.
- 20 SEQ ID NO: 166 is the amino acid sequence encoded by SEQ ID NO: 164.
- SEQ ID NO: 167 is the full-length cDNA sequence of a first variant of L762P.
- SEQ ID NO: 168 is the full-length cDNA sequence of a second variant of L762P.
- SEQ ID NO: 169 is the amino acid sequence encoded by SEQ ID NO: 167.
- SEQ ID NO: 170 is the amino acid sequence encoded by SEQ ID NO: 168.
- 25 SEQ ID NO: 171 is the full-length cDNA sequence for L773P (also referred to as contig 56).
- SEQ ID NO: 172 is the amino acid sequence encoded by SEQ ID NO: 171.
- SEQ ID NO: 173 is an extended cDNA sequence for L519S.
- SEQ ID NO: 174 is the predicted amino acid sequence encoded by SEQ ID NO: 174.
- 30 SEQ ID NO: 175 is the full-length cDNA sequence for L523S.
- SEQ ID NO: 176 is the predicted amino acid sequence encoded by SEQ ID NO: 175.

- SEQ ID NO: 177 is the determined cDNA sequence for LST-sub5-7A.
- SEQ ID NO: 178 is the determined cDNA sequence for LST-sub5-8G.
- SEQ ID NO: 179 is the determined cDNA sequence for LST-sub5-8H.
- SEQ ID NO: 180 is the determined cDNA sequence for LST-sub5-10B.
- 5 SEQ ID NO: 181 is the determined cDNA sequence for LST-sub5-10H.
- SEQ ID NO: 182 is the determined cDNA sequence for LST-sub5-12B.
- SEQ ID NO: 183 is the determined cDNA sequence for LST-sub5-11C.
- SEQ ID NO: 184 is the determined cDNA sequence for LST-sub6-1c.
- SEQ ID NO: 185 is the determined cDNA sequence for LST-sub6-2f.
- 10 SEQ ID NO: 186 is the determined cDNA sequence for LST-sub6-2G.
- SEQ ID NO: 187 is the determined cDNA sequence for LST-sub6-4d.
- SEQ ID NO: 188 is the determined cDNA sequence for LST-sub6-4e.
- SEQ ID NO: 189 is the determined cDNA sequence for LST-sub6-4f.
- SEQ ID NO: 190 is the determined cDNA sequence for LST-sub6-3h.
- 15 SEQ ID NO: 191 is the determined cDNA sequence for LST-sub6-5d.
- SEQ ID NO: 192 is the determined cDNA sequence for LST-sub6-5h.
- SEQ ID NO: 193 is the determined cDNA sequence for LST-sub6-6h.
- SEQ ID NO: 194 is the determined cDNA sequence for LST-sub6-7a.
- SEQ ID NO: 195 is the determined cDNA sequence for LST-sub6-8a.
- 20 SEQ ID NO: 196 is the determined cDNA sequence for LST-sub6-7d.
- SEQ ID NO: 197 is the determined cDNA sequence for LST-sub6-7e.
- SEQ ID NO: 198 is the determined cDNA sequence for LST-sub6-8e.
- SEQ ID NO: 199 is the determined cDNA sequence for LST-sub6-7g.
- SEQ ID NO: 200 is the determined cDNA sequence for LST-sub6-9f.
- 25 SEQ ID NO: 201 is the determined cDNA sequence for LST-sub6-9h.
- SEQ ID NO: 202 is the determined cDNA sequence for LST-sub6-11b.
- SEQ ID NO: 203 is the determined cDNA sequence for LST-sub6-11c.
- SEQ ID NO: 204 is the determined cDNA sequence for LST-sub6-12c.
- SEQ ID NO: 205 is the determined cDNA sequence for LST-sub6-12e.
- 30 SEQ ID NO: 206 is the determined cDNA sequence for LST-sub6-12f.
- SEQ ID NO: 207 is the determined cDNA sequence for LST-sub6-11g.

- SEQ ID NO: 208 is the determined cDNA sequence for LST-sub6-12g.
- SEQ ID NO: 209 is the determined cDNA sequence for LST-sub6-12h.
- SEQ ID NO: 210 is the determined cDNA sequence for LST-sub6-II-1a.
- SEQ ID NO: 211 is the determined cDNA sequence for LST-sub6-II-2b.
- 5 SEQ ID NO: 212 is the determined cDNA sequence for LST-sub6-II-2g.
- SEQ ID NO: 213 is the determined cDNA sequence for LST-sub6-II-1h.
- SEQ ID NO: 214 is the determined cDNA sequence for LST-sub6-II-4a.
- SEQ ID NO: 215 is the determined cDNA sequence for LST-sub6-II-4b.
- SEQ ID NO: 216 is the determined cDNA sequence for LST-sub6-II-3e.
- 10 SEQ ID NO: 217 is the determined cDNA sequence for LST-sub6-II-4f.
- SEQ ID NO: 218 is the determined cDNA sequence for LST-sub6-II-4g.
- SEQ ID NO: 219 is the determined cDNA sequence for LST-sub6-II-4h.
- SEQ ID NO: 220 is the determined cDNA sequence for LST-sub6-II-5c.
- SEQ ID NO: 221 is the determined cDNA sequence for LST-sub6-II-5e.
- 15 SEQ ID NO: 222 is the determined cDNA sequence for LST-sub6-II-6f.
- SEQ ID NO: 223 is the determined cDNA sequence for LST-sub6-II-5g.
- SEQ ID NO: 224 is the determined cDNA sequence for LST-sub6-II-6g.
- SEQ ID NO: 225 is the amino acid sequence for L528S.
- SEQ ID NO: 226-251 are synthetic peptides derived from L762P.
- 20 SEQ ID NO: 252 is the expressed amino acid sequence of L514S.
- SEQ ID NO: 253 is the DNA sequence corresponding to SEQ ID NO: 252.
- SEQ ID NO: 254 is the DNA sequence of a L762P expression construct.
- SEQ ID NO: 255 is the determined cDNA sequence for clone 23785.
- SEQ ID NO: 256 is the determined cDNA sequence for clone 23786.
- 25 SEQ ID NO: 257 is the determined cDNA sequence for clone 23788.
- SEQ ID NO: 258 is the determined cDNA sequence for clone 23790.
- SEQ ID NO: 259 is the determined cDNA sequence for clone 23793.
- SEQ ID NO: 260 is the determined cDNA sequence for clone 23794.
- SEQ ID NO: 261 is the determined cDNA sequence for clone 23795.
- 30 SEQ ID NO: 262 is the determined cDNA sequence for clone 23796.
- SEQ ID NO: 263 is the determined cDNA sequence for clone 23797.

- SEQ ID NO: 264 is the determined cDNA sequence for clone 23798.
SEQ ID NO: 265 is the determined cDNA sequence for clone 23799.
SEQ ID NO: 266 is the determined cDNA sequence for clone 23800.
SEQ ID NO: 267 is the determined cDNA sequence for clone 23802.
5 SEQ ID NO: 268 is the determined cDNA sequence for clone 23803.
SEQ ID NO: 269 is the determined cDNA sequence for clone 23804.
SEQ ID NO: 270 is the determined cDNA sequence for clone 23805.
SEQ ID NO: 271 is the determined cDNA sequence for clone 23806.
SEQ ID NO: 272 is the determined cDNA sequence for clone 23807.
10 SEQ ID NO: 273 is the determined cDNA sequence for clone 23808.
SEQ ID NO: 274 is the determined cDNA sequence for clone 23809.
SEQ ID NO: 275 is the determined cDNA sequence for clone 23810.
SEQ ID NO: 276 is the determined cDNA sequence for clone 23811.
SEQ ID NO: 277 is the determined cDNA sequence for clone 23812.
15 SEQ ID NO: 278 is the determined cDNA sequence for clone 23813.
SEQ ID NO: 279 is the determined cDNA sequence for clone 23815.
SEQ ID NO: 280 is the determined cDNA sequence for clone 25298.
SEQ ID NO: 281 is the determined cDNA sequence for clone 25299.
SEQ ID NO: 282 is the determined cDNA sequence for clone 25300.
20 SEQ ID NO: 283 is the determined cDNA sequence for clone 25301.
SEQ ID NO: 284 is the determined cDNA sequence for clone 25304.
SEQ ID NO: 285 is the determined cDNA sequence for clone 25309.
SEQ ID NO: 286 is the determined cDNA sequence for clone 25312.
SEQ ID NO: 287 is the determined cDNA sequence for clone 25317.
25 SEQ ID NO: 288 is the determined cDNA sequence for clone 25321.
SEQ ID NO: 289 is the determined cDNA sequence for clone 25323.
SEQ ID NO: 290 is the determined cDNA sequence for clone 25327.
SEQ ID NO: 291 is the determined cDNA sequence for clone 25328.
SEQ ID NO: 292 is the determined cDNA sequence for clone 25332.
30 SEQ ID NO: 293 is the determined cDNA sequence for clone 25333.
SEQ ID NO: 294 is the determined cDNA sequence for clone 25336.

- SEQ ID NO: 295 is the determined cDNA sequence for clone 25340.
- SEQ ID NO: 296 is the determined cDNA sequence for clone 25342.
- SEQ ID NO: 297 is the determined cDNA sequence for clone 25356.
- SEQ ID NO: 298 is the determined cDNA sequence for clone 25357.
- 5 SEQ ID NO: 299 is the determined cDNA sequence for clone 25361.
- SEQ ID NO: 300 is the determined cDNA sequence for clone 25363.
- SEQ ID NO: 301 is the determined cDNA sequence for clone 25397.
- SEQ ID NO: 302 is the determined cDNA sequence for clone 25402.
- SEQ ID NO: 303 is the determined cDNA sequence for clone 25403.
- 10 SEQ ID NO: 304 is the determined cDNA sequence for clone 25405.
- SEQ ID NO: 305 is the determined cDNA sequence for clone 25407.
- SEQ ID NO: 306 is the determined cDNA sequence for clone 25409.
- SEQ ID NO: 307 is the determined cDNA sequence for clone 25396.
- SEQ ID NO: 308 is the determined cDNA sequence for clone 25414.
- 15 SEQ ID NO: 309 is the determined cDNA sequence for clone 25410.
- SEQ ID NO: 310 is the determined cDNA sequence for clone 25406.
- SEQ ID NO: 311 is the determined cDNA sequence for clone 25306.
- SEQ ID NO: 312 is the determined cDNA sequence for clone 25362.
- SEQ ID NO: 313 is the determined cDNA sequence for clone 25360.
- 20 SEQ ID NO: 314 is the determined cDNA sequence for clone 25398.
- SEQ ID NO: 315 is the determined cDNA sequence for clone 25355.
- SEQ ID NO: 316 is the determined cDNA sequence for clone 25351.
- SEQ ID NO: 317 is the determined cDNA sequence for clone 25331.
- SEQ ID NO: 318 is the determined cDNA sequence for clone 25338.
- 25 SEQ ID NO: 319 is the determined cDNA sequence for clone 25335.
- SEQ ID NO: 320 is the determined cDNA sequence for clone 25329.
- SEQ ID NO: 321 is the determined cDNA sequence for clone 25324.
- SEQ ID NO: 322 is the determined cDNA sequence for clone 25322.
- SEQ ID NO: 323 is the determined cDNA sequence for clone 25319.
- 30 SEQ ID NO: 324 is the determined cDNA sequence for clone 25316.
- SEQ ID NO: 325 is the determined cDNA sequence for clone 25311.

- SEQ ID NO: 326 is the determined cDNA sequence for clone 25310.
- SEQ ID NO: 327 is the determined cDNA sequence for clone 25302.
- SEQ ID NO: 328 is the determined cDNA sequence for clone 25315.
- SEQ ID NO: 329 is the determined cDNA sequence for clone 25308.
- 5 SEQ ID NO: 330 is the determined cDNA sequence for clone 25303.
- SEQ ID NO: 331-337 are the cDNA sequences of isoforms of the p53 tumor suppressor homologue, p63 (also referred to as L530S).
- SEQ ID NO: 338-344 are the amino acid sequences encoded by SEQ ID NO: 331-337, respectively.
- 10 SEQ ID NO: 345 is a second cDNA sequence for the antigen L763P.
- SEQ ID NO: 346 is the amino acid sequence encoded by the sequence of SEQ ID NO: 345.
- SEQ ID NO: 347 is a determined full-length cDNA sequence for L523S.
- SEQ ID NO: 348 is the predicted amino acid sequence encoded by SEQ ID NO: 347.
- 15 SEQ ID NO: 349 is the cDNA sequence encoding the N-terminal portion of L773P.
- SEQ ID NO: 350 is the amino acid sequence of the N-terminal portion of L773P.

DETAILED DESCRIPTION OF THE INVENTION

- As noted above, the present invention is generally directed to
- 20 compositions and methods for the therapy and diagnosis of cancer, such as lung cancer. The compositions described herein may include lung tumor polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (e.g., T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic
- 25 portion) of a lung tumor protein or a variant thereof. A "lung tumor protein" is a protein that is expressed in lung tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a normal tissue, as determined using a representative assay provided herein. Certain lung tumor proteins are tumor proteins that react detectably (within an immunoassay, such as an ELISA or Western
- 30 blot) with antisera of a patient afflicted with lung cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of

such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

The present invention is based on the discovery human lung tumor proteins. Sequences of polynucleotides encoding specific tumor proteins are provided in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349.

LUNG TUMOR PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a lung tumor protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a lung tumor protein. More preferably, a polynucleotide encodes an immunogenic portion of a lung tumor protein. Polynucleotides complementary to any such sequences are also encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a lung tumor protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the immunogenicity of the

encoded polypeptide is not diminished, relative to a native tumor protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native lung tumor protein or a portion thereof. The term "variants" also encompasses homologous genes of xenogenic origin.

Two polynucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins - Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy - the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad. Sci. USA* 80:726-730.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20

positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (i.e. gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (i.e. the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

10 Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native lung tumor protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; 15 followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal 20 homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous 25 genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. 30 For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (i.e., expression that

is at least two fold greater in a lung tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and
5 Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as lung tumor cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

10 An amplified portion may be used to isolate a full length gene from a suitable library (e.g., a lung tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be
15 preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (e.g., by nick-translation or end-labeling with ^{32}P) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured
20 bacterial colonies (or lawns containing phage plaques) with the labeled probe (see Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using
25 a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into a single contiguous sequence. A full length cDNA molecule can be
30 generated by ligating suitable fragments, using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (see Triglia et al., *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (e.g., NCBI BLAST searches), and such ESTs

may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

Certain nucleic acid sequences of cDNA molecules encoding portions of lung tumor proteins are provided in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis. Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (see Adelman et al., *DNA* 2:183, 1983). Alternatively, RNA molecules may be generated by *in vitro* or *in vivo* transcription of DNA sequences encoding a lung tumor protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated *in vivo* (e.g. by transfecting antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a lung tumor polypeptide, and administering the transfected cells to the patient).

A portion of a sequence complementary to a coding sequence (i.e., an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a tumor protein. Antisense technology can be used to control gene expression through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (see Gee et al., *In Huber and Carr, Molecular and Immunologic Approaches*, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (e.g., promoter, enhancer or transcription

initiation site), and block transcription of the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled
5 with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability *in vivo*.
10 Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl- methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

15 Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation
20 vectors and sequencing vectors. In general, a vector will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to
25 permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not
30 limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (e.g., avian pox virus). The polynucleotides may also be administered as naked

plasmid vectors. Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane vesicle). The preparation and use of such systems is well known in the art.

15 LUNG TUMOR POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a lung tumor protein or a variant thereof, as described herein. As noted above, a "lung tumor protein" is a protein that is expressed by lung tumor cells. Proteins that are lung tumor proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with lung cancer. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a lung tumor protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may

contain a small N- and/or C-terminal deletion (e.g., 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (i.e., they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native lung tumor protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (e.g., in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ¹²⁵I-labeled Protein A.

As noted above, a composition may comprise a variant of a native lung tumor protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native lung tumor protein in one or more substitutions, deletions, additions and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein. Preferred variants include

those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (e.g., 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein.

5 Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydropathic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the

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polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast, higher eukaryotic and plant cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans,

or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second

polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (*see, for example, Stoute et al. New Engl. J. Med.*, 336:86-91, 1997).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible

for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (see 5 *Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides 10 as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is 15 considered to be isolated if, for example, it is cloned into a vector that is not a part of the natural environment.

BINDING AGENTS

The present invention further provides agents, such as antibodies and 20 antigen-binding fragments thereof, that specifically bind to a lung tumor protein. As used herein, an antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a lung tumor protein if it reacts at a detectable level (within, for example, an ELISA) with a lung tumor protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association 25 between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding 30 constant for complex formation exceeds about 10^3 L/mol. The binding constant may be determined using methods well known in the art.

Binding agents may be further capable of differentiating between patients with and without a cancer, such as lung cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a lung tumor protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (e.g., blood, sera, sputum urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically.

Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.*, reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be prepared using standard techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane,

Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include ^{90}Y , ^{123}I , ^{125}I , ^{131}I , ^{186}Re , ^{188}Re , ^{211}At , and ^{212}Bi . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (e.g., covalently bonded) to a suitable monoclonal antibody either directly or indirectly (e.g., via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (e.g., a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, e.g., U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (e.g., U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (e.g., U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (e.g., U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (e.g., U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (e.g., U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (e.g., U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (e.g., U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (e.g., U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

T CELLS

Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a lung tumor protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the Isolex™ System, available from Nexell Therapeutics, Inc. Irvine, CA (see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a lung tumor polypeptide, polynucleotide encoding a lung tumor polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a lung tumor polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a lung tumor polypeptide if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell

proliferation can be detected by measuring an increased rate of DNA synthesis (e.g., by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a lung tumor polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN-γ) is indicative of T cell activation (see Coligan et al., Current Protocols in Immunology, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a lung tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4⁺ and/or CD8⁺. Lung tumor protein-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4⁺ or CD8⁺ T cells that proliferate in response to a lung tumor polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a lung tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a lung tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of a lung tumor protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (i.e., vaccines). Pharmaceutical compositions comprise one or more such compounds and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and an immunostimulant. An immunostimulant

may be any substance that enhances or potentiates an immune response to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (e.g., polylactic galactide) and liposomes (into which the compound is incorporated; see e.g., Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995).

Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein.

Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (e.g., vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus.

Suitable systems are disclosed, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl.*

Acad. Sci. USA 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., *Science* 5 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier 10 will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. 15 For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres 20 are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Such compositions may also comprise buffers (e.g., neutral buffered saline or phosphate buffered saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA or glutathione, adjuvants (e.g., aluminum hydroxide) 25 and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of immunostimulants may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a 30 substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A,

Bordetella pertussis or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA);
5 aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

10 Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN- γ , TNF α , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6 and IL-10) tend to favor the
15 induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using
20 standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt.
25 MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT) (see US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555 and WO 99/33488. Immunostimulatory DNA sequences
30 are also described, for example, by Sato et al., *Science* 273:352, 1996. Another preferred adjuvant is a saponin, preferably QS21 (Aquila Biopharmaceuticals Inc.,

Framingham, MA), which may be used alone or in combination with other adjuvants. For example, an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210.

Other preferred adjuvants include Montanide ISA 720 (Seppic, France), SAF (Chiron, California, United States), ISCOMS (CSL), MF-59 (Chiron), the SBAS series of adjuvants (e.g., SBAS-2 or SBAS-4, available from SmithKline Beecham, Rixensart, Belgium), Detox (Ribi ImmunoChem Research Inc., Hamilton, MT), RC-529 (Ribi ImmunoChem Research Inc., Hamilton, MT) and Aminoalkyl glucosaminide 4-phosphates (AGPs).

Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient. The compositions described herein may be administered as part of a sustained release formulation (i.e., a formulation such as a capsule, sponge or gel (composed of polysaccharides, for example) that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology (see, e.g. Coombes et al., *Vaccine* 14:1429-1438, 1996) and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix and/or contained within a reservoir surrounded by a rate controlling membrane.

Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. Such carriers include microparticles of poly(lactide-co-glycolide), as well as polyacrylate, latex, starch, cellulose and dextran. Other delayed-release carriers include supramolecular biovectors, which comprise a non-liquid hydrophilic core (e.g., a cross-linked polysaccharide or oligosaccharide) and, optionally,

an external layer comprising an amphiphilic compound, such as a phospholipid (see e.g., U.S. Patent No. 5,151,254 and PCT applications WO 94/20078, WO/94/23701 and WO 96/06638). The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (see Timmerman and Levy, *Ann. Rev. Med.* 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take up, process and present antigens with high efficiency, and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (see Zitvogel et al., *Nature Med.* 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood,

bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF α to cultures of monocytes
5 harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF α , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

10 Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which
15 correlates with the high expression of Fc γ receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (e.g., CD54 and CD11) and costimulatory molecules (e.g., CD40, CD80, CD86 and 4-1BB).

20 APCs may generally be transfected with a polynucleotide encoding a lung tumor protein (or portion or other variant thereof) such that the lung tumor polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein.

25 Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell*
30 *Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the lung tumor polypeptide, DNA

(naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (e.g., vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (e.g., a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

Vaccines and pharmaceutical compositions may be presented in unit-dose or multi-dose containers, such as sealed ampoules or vials. Such containers are preferably hermetically sealed to preserve sterility of the formulation until use. In general, formulations may be stored as suspensions, solutions or emulsions in oily or aqueous vehicles. Alternatively, a vaccine or pharmaceutical composition may be stored in a freeze-dried condition requiring only the addition of a sterile liquid carrier immediately prior to use.

15 CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as lung cancer. Within such methods, pharmaceutical compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8⁺ cytotoxic T lymphocytes and CD4⁺ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast and/or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow *in vivo* and to survive

long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see, for example, Cheever et al., Immunological Reviews 157:177, 1997*).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25 μ g to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free

survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a lung tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or more lung tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, sputum urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as lung cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a lung tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue.

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent

that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full length lung tumor proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10 μ g, and preferably about 100 ng to about 1 μ g, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the

binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (see, e.g., Pierce Immunotechnology Catalog and Handbook, 1991, at 5 A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. 10 Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

15 More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to 20 bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (i.e., incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with lung cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of 25 that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

30 Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second

antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide.

5 An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are
10 generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of
15 the reaction products.

To determine the presence or absence of a cancer, such as lung cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average
20 mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical*
25 *Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (i.e., sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (i.e., the value that
30 encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered

positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

5 In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution
10 containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent.
15 Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the
20 biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1 μ g, and more preferably from about 50 ng to about
25 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to
30 those of ordinary skill in the art that the above protocols may be readily modified to use lung tumor polypeptides to detect antibodies that bind to such polypeptides in a

biological sample. The detection of such lung tumor protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a lung tumor protein in a biological sample. Within certain methods, a biological sample comprising CD4⁺ and/or CD8⁺ T cells isolated from a patient is incubated with a lung tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with polypeptide (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of lung tumor polypeptide to serve as a control. For CD4⁺ T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8⁺ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a lung tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a lung tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (i.e., hybridizes to) a polynucleotide encoding the lung tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a lung tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%,

preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a lung tumor protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes will hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349. Techniques for both PCR based assays and hybridization assays are well known in the art (*see, for example, Mullis et al., Cold Spring Harbor Symp. Quant. Biol., 51:263, 1987; Erlich ed., PCR Technology, Stockton Press, NY, 1989*).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the

level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor.

- 5 One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

- As noted above, to improve sensitivity, multiple lung tumor protein
10 markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins
15 provided herein may be combined with assays for other known tumor antigens.

DIAGNOSTIC KITS

- The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components
20 necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a lung tumor protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements,
25 such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

- Alternatively, a kit may be designed to detect the level of mRNA encoding a lung tumor protein in a biological sample. Such kits generally comprise at
30 least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a lung tumor protein. Such an oligonucleotide may be used,

for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a lung tumor protein.

The following Examples are offered by way of illustration and not by way of limitation.

EXAMPLE 1

ISOLATION AND CHARACTERIZATION OF cDNA SEQUENCES
ENCODING LUNG TUMOR POLYPEPTIDES

5 This example illustrates the isolation of cDNA molecules encoding lung tumor-specific polypeptides from lung tumor cDNA libraries.

A. ISOLATION OF cDNA SEQUENCES FROM A LUNG SQUAMOUS CELL
10 CARCINOMA LIBRARY

A human lung squamous cell carcinoma cDNA expression library was constructed from poly A⁺ RNA from a pool of two patient tissues using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD) following the manufacturer's protocol. Specifically, lung carcinoma
15 tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A⁺ RNA was then purified using an oligo dT cellulose column as described in Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989. First-strand cDNA was
20 synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with BstXI/EcoRI adaptors (Invitrogen, San Diego, CA) and digested with NotI. Following size fractionation with cDNA size fractionation columns (BRL Life Technologies), the cDNA was ligated into the BstXI/NotI site of pcDNA3.1 (Invitrogen) and transformed into ElectroMax *E. coli* DH10B cells (BRL Life
25 Technologies) by electroporation.

Using the same procedure, a normal human lung cDNA expression library was prepared from a pool of four tissue specimens. The cDNA libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The lung
30 squamous cell carcinoma library contained 2.7×10^6 independent colonies, with 100% of clones having an insert and the average insert size being 2100 base pairs. The normal

lung cDNA library contained 1.4×10^6 independent colonies, with 90% of clones having inserts and the average insert size being 1800 base pairs. For both libraries, sequence analysis showed that the majority of clones had a full-length cDNA sequence and were synthesized from mRNA.

5 cDNA library subtraction was performed using the above lung squamous cell carcinoma and normal lung cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some modifications. Specifically, a lung squamous cell carcinoma-specific subtracted cDNA library was generated as follows. Normal tissue cDNA library (80 μ g) was digested with BamHI and XhoI, followed by a filling-in
10 reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 133 μ l of H₂O, heat-denatured and mixed with 133 μ l (133 μ g) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (67 μ l) was added
15 and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23 μ l H₂O to form the driver DNA.
To form the tracer DNA, 10 μ g lung squamous cell carcinoma cDNA library was digested with NotI and SpeI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech, Palo Alto, CA). Typically, 5 μ g of
20 cDNA was recovered after the sizing column. Following ethanol precipitation, the tracer DNA was dissolved in 5 μ l H₂O. Tracer DNA was mixed with 15 μ l driver DNA and 20 μ l of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and
25 incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12 μ l H₂O, mixed with 8 μ l driver DNA and 20 μ l of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After
30 removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into NotI/SpeI site of chloramphenicol resistant pBCSK⁺ (Stratagene, La Jolla, CA) and

transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a lung squamous cell carcinoma specific subtracted cDNA library (herein after referred to as "lung subtraction I").

A second lung squamous cell carcinoma specific subtracted cDNA library (referred to as "lung subtraction II") was generated in a similar way to the lung subtraction library I, except that eight frequently recovered genes from lung subtraction I were included in the driver DNA, and 24,000 independent clones were recovered.

To analyze the subtracted cDNA libraries, plasmid DNA was prepared from 320 independent clones, randomly picked from the subtracted lung squamous cell carcinoma specific libraries. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A and/or Model 377 (Foster City, CA). The cDNA sequences for sixty isolated clones are provided in SEQ ID NO: 1-60. These sequences were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). No significant homologies were found to the sequences provided in SEQ ID NO: 2, 3, 19, 38 and 46. The sequences of SEQ ID NO: 1, 6-8, 10-13, 15, 17, 18, 20-27, 29, 30, 32, 34-37, 39-45, 47-49, 51, 52, 54, 55 and 57-59 were found to show some homology to previously identified expressed sequence tags (ESTs). The sequences of SEQ ID NO: 9, 28, 31 and 33 were found to show some homology to previously identified non-human gene sequences and the sequences of SEQ ID NO: 4, 5, 14, 50, 53, 56 and 60 were found to show some homology to gene sequences previously identified in humans.

The subtraction procedure described above was repeated using the above lung squamous cell carcinoma cDNA library as the tracer DNA, and the above normal lung tissue cDNA library and a cDNA library from normal liver and heart (constructed from a pool of one sample of each tissue as described above), plus twenty other cDNA clones that were frequently recovered in lung subtractions I and II, as the driver DNA (lung subtraction III). The normal liver and heart cDNA library contained 1.76×10^6 independent colonies, with 100% of clones having inserts and the average insert size being 1600 base pairs. Ten additional clones were isolated (SEQ ID NO: 61-70). Comparison of these cDNA sequences with those in the gene bank as described above,

revealed no significant homologies to the sequences provided in SEQ ID NO: 62 and 67. The sequences of SEQ ID NO: 61, 63-66, 68 and 69 were found to show some homology to previously isolated ESTs and the sequence provided in SEQ ID NO: 70 was found to show some homology to a previously identified rat gene.

5 In further studies, the subtraction procedure described above was repeated using the above lung squamous cell carcinoma cDNA library as the tracer DNA, and a cDNA library from a pool of normal lung, kidney, colon, pancreas, brain, resting PBMC, heart, skin and esophagus as the driver DNA, with esophagus cDNAs making up one third of the driver material. Since esophagus is enriched in normal
10 epithelial cells, including differentiated squamous cells, this procedure is likely to enrich genes that are tumor specific rather than tissues specific. The cDNA sequences of 48 clones determined in this subtraction are provided in SEQ ID NO: 177-224. The sequences of SEQ ID NO: 177, 178, 180, 181, 183, 187, 192, 195-197, 208, 211, 212, 215, 216, 218 and 219 showed some homology to previously identified genes. The
15 sequences of SEQ ID NO: 179, 182, 184-186, 188-191, 193, 194, 198-207, 209 210, 213, 214, 217, 220 and 224 showed some homology to previously determined ESTs. The sequence of SEQ ID NO: 221-223 showed no homology to any previously determined sequence.

20 B. ISOLATION OF cDNA SEQUENCES FROM A LUNG ADENOCARCINOMA LIBRARY

A human lung adenocarcinoma cDNA expression library was constructed as described above. The library contained 3.2×10^6 independent colonies, with 100% of clones having an insert and the average insert size being 1500 base pairs.
25 Library subtraction was performed as described above using the normal lung and normal liver and heart cDNA expression libraries described above as the driver DNA. Twenty-six hundred independent clones were recovered.

Initial cDNA sequence analysis from 100 independent clones revealed many ribosomal protein genes. The cDNA sequences for fifteen clones isolated in this
30 subtraction are provided in SEQ ID NO: 71-86. Comparison of these sequences with those in the gene bank as described above revealed no significant homologies to the

sequence provided in SEQ ID NO: 84. The sequences of SEQ ID NO: 71, 73, 74, 77, 78 and 80-82 were found to show some homology to previously isolated ESTs, and the sequences of SEQ ID NO: 72, 75, 76, 79, 83 and 85 were found to show some homology to previously identified human genes.

5 In further studies, a cDNA library (referred to as mets3616A) was constructed from a metastatic lung adenocarcinoma. The determined cDNA sequences of 25 clones sequenced at random from this library are provided in SEQ ID NO: 255-279. The mets3616A cDNA library was subtracted against a cDNA library prepared from a pool of normal lung, liver, pancreas, skin, kidney, brain and resting PBMC. To
10 increase the specificity of the subtraction, the driver was spiked with genes that were determined to be most abundant in the mets3616A cDNA library, such as EF1-alpha, integrin-beta and anticoagulant protein PP4, as well as with cDNAs that were previously found to be differentially expressed in subtracted lung adenocarcinoma cDNA libraries. The determined cDNA sequences of 51 clones isolated from the
15 subtracted library (referred to as mets3616A-S1) are provided in SEQ ID NO: 280-330.

Comparison of the sequences of SEQ ID NO: 255-330 with those in the public databases revealed no significant homologies to the sequences of SEQ ID NO: 255-258, 260, 262-264, 270, 272, 275, 276, 279, 281, 287, 291, 296, 300 and 310. The sequences of SEQ ID NO: 259, 261, 265-269, 271, 273, 274, 277, 278, 282-285, 288-
20 290, 292, 294, 297-299, 301, 303-309, 313, 314, 316, 320-324 and 326-330 showed some homology to previously identified gene sequences, while the sequences of SEQ ID NO: 280, 286, 293, 302, 310, 312, 315, 317-319 and 325 showed some homology to previously isolated expressed sequence tags (ESTs).

25

EXAMPLE 2

DETERMINATION OF TISSUE SPECIFICITY OF LUNG TUMOR

POLYPEPTIDES

Using gene specific primers, mRNA expression levels for seven
30 representative lung tumor polypeptides described in Example 1 were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 2 µg of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR, β-actin was used as an internal control for each of the tissues examined. 1 µl of 1:30 dilution of cDNA was employed to enable the linear range amplification of the β-actin template and was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the β-actin levels were determined for each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in five different types of tumor tissue (lung squamous cell carcinoma from 3 patients, lung adenocarcinoma, colon tumor from 2 patients, breast tumor and prostate tumor), and thirteen different normal tissues (lung from 4 donors, prostate, brain, kidney, liver, ovary, skeletal muscle, skin, small intestine, stomach, myocardium, retina and testes). Using a 10-fold amount of cDNA, the antigen LST-S1-90 (SEQ ID NO: 3) was found to be expressed at high levels in lung squamous cell carcinoma and in breast tumor, and at low to undetectable levels in the other tissues examined.

The antigen LST-S2-68 (SEQ ID NO: 15) appears to be specific to lung and breast tumor, however, expression was also detected in normal kidney. Antigens LST-S1-169 (SEQ ID NO: 6) and LST-S1-133 (SEQ ID NO: 5) appear to be very abundant in lung tissues (both normal and tumor), with the expression of these two genes being decreased in most of the normal tissues tested. Both LST-S1-169 and LST-S1-133 were also expressed in breast and colon tumors. Antigens LST-S1-6 (SEQ ID NO: 7) and LST-S2-I2-5F (SEQ ID NO: 47) did not show tumor or tissue specific expression, with the expression of LST-S1-28 being rare and only detectable in a few tissues. The antigen LST-S3-7 (SEQ ID NO: 63) showed lung and breast tumor specific expression, with its message only being detected in normal testes when the PCR was performed for 30 cycles. Lower level expression was detected in some

normal tissues when the cycle number was increased to 35. Antigen LST-S3-13 (SEQ ID NO: 66) was found to be expressed in 3 out of 4 lung tumors, one breast tumor and both colon tumor samples. Its expression in normal tissues was lower compared to tumors, and was only detected in 1 out of 4 normal lung tissues and in normal tissues from kidney, ovary and retina. Expression of antigens LST-S3-4 (SEQ ID NO: 62) and LST-S3-14 (SEQ ID NO: 67) was rare and did not show any tissue or tumor-specificity. Consistent with Northern blot analyses, the RT-PCT results on antigen LAT-S1-A-10A (SEQ ID NO: 78) suggested that its expression is high in lung, colon, stomach and small intestine tissues, including lung and colon tumors, whereas its expression was low or undetectable in other tissues.

A total of 2002 cDNA fragments isolated in lung subtractions I, II and III, described above, were colony PCR amplified and their mRNA expression levels in lung tumor, normal lung, and various other normal and tumor tissues were determined using microarray technology (Synteni, Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Seventeen non-redundant cDNA clones showed over-expression in lung squamous tumors, with expression in normal tissues tested (lung, skin, lymph node, colon, liver, pancreas, breast, heart, bone marrow, large intestine, kidney, stomach, brain, small intestine, bladder and salivary gland) being either undetectable, or 10-fold less compared to lung squamous tumors. The determined partial cDNA sequences for the clone L513S are provided in SEQ ID NO: 87 and 88; those for L514S are provided in SEQ ID NO: 89 and 90; those for L516S in SEQ ID NO: 91 and 92; that for L517S in SEQ ID NO: 93; that for L519S in SEQ ID NO: 94; those for L520S in SEQ ID NO: 95 and 96; those for L521S in SEQ ID NO: 97 and 98; that for L522S in SEQ ID NO: 99; that for L523S in SEQ ID NO: 100; that for L524S in SEQ ID NO: 101; that for L525S in SEQ ID NO: 102; that for L526S in SEQ ID NO: 103; that for L527S in SEQ ID NO: 104; that for L528S in SEQ ID NO: 105; that for L529S in SEQ ID NO: 106;

and those for L530S in SEQ ID NO: 107 and 108. Additionally, the full-length cDNA sequence for L530S is provided in SEQ ID NO: 151, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 152. L530S shows homology to a splice variant of a p53 tumor suppressor homologue, p63. The cDNA sequences of 7 known isoforms of p63 are provided in SEQ ID NO: 331-337, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 338-344, respectively.

Due to polymorphisms, the clone L531S appears to have two forms. A first determined full-length cDNA sequence for L531S is provided in SEQ ID NO: 109, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 110. A second determined full-length cDNA sequence for L531S is provided in SEQ ID NO: 111, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 112. The sequence of SEQ ID NO: 111 is identical to that of SEQ ID NO: 109, except that it contains a 27 bp insertion. Similarly, L514S also has two alternatively spliced forms; the first variant cDNA is listed as SEQ ID NO: 153, with the corresponding amino acid sequence being provided in SEQ ID NO: 155. The second variant form of L514S full-length cDNA is provided in SEQ ID NO: 154, with its corresponding amino acid sequence being provided in SEQ ID NO: 156.

Full length cloning for L524S (SEQ ID NO: 101) yielded two variants (SEQ ID NO: 163 and 164) with the corresponding predicted amino acid sequences of SEQ ID NO: 165 and 166, respectively. Both variants have been shown to encode parathyroid hormone-related peptide.

Attempts to isolate the full-length cDNA for L519S, resulted in the isolation of the extended cDNA sequence provided in SEQ ID NO: 173, which contains a potential open reading frame. The predicted amino acid sequence encoded by the sequence of SEQ ID NO: 173 is provided in SEQ ID NO: 174. Additionally, the full-length cDNA sequence for the clone of SEQ ID NO: 100 (known as L523S), a known gene, is provided in SEQ ID NO: 175, with the corresponding predicted amino acid sequence provided in SEQ ID NO: 176. In further studies, a full-length cDNA sequence for L523S was isolated from a L523S-positive tumor cDNA library by PCR amplification using gene specific primers designed from the sequence of SEQ ID NO: 175. The determined cDNA sequence is provided in SEQ ID NO: **. The amino acid

sequence encoded by this sequence is provided in SEQ ID NO: **. This protein sequence differs from the previously published protein sequence at two amino acid positions, namely at positions 158 and 410.

Comparison of the sequences of L514S and L531S (SEQ ID NO: 87 and 88, 89 and 90, and 109, respectively) with those in the gene bank, as described above, revealed no significant homologies to known sequences. The sequences of L513S, L516S, L517S, L519S, L520S and L530S (SEQ ID NO: 87 and 88, 91 and 92, 93, 94, 95 and 96, 107 and 108, respectively) were found to show some homology to previously identified ESTs. The sequences of L521S, L522S, L523S, L524S, L525S, L526S, L527S, L528S and L529S (SEQ ID NO: 97 and 98, 99, 99, 101, 102, 103, 104, 105, and 106, respectively) were found to represent known genes. The determined full-length cDNA sequences for L520S is provided in SEQ ID NO: 113, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 114. Subsequent microarray analysis has shown L520S to be overexpressed in breast tumors in addition to lung squamous tumors.

Further analysis has demonstrated that L529S (SEQ ID NO: 106 and 115), L525S (SEQ ID NO: 102 and 120) and L527S (SEQ ID NO: 104) are cytoskeletal components and potentially squamous cell specific proteins. L529S is connexin 26, a gap junction protein. It is highly expressed in lung squamous tumor 9688T, and moderately over-expressed in two others. However, lower level expression of connexin 26 is also detectable in normal skin, colon, liver and stomach. The over-expression of connexin 26 in some breast tumors has been reported and a mutated form of L529S may result in over-expression in lung tumors. L525S is plakophilin 1, a desmosomal protein found in plaque-bearing adhering junctions of the skin. Expression levels for L525S mRNA is highly elevated in three out of four lung squamous tumors tested, and in normal skin. L527S has been identified as keratin 6 isoform, type II 58 Kd keratin, and cytokeratin 13 and shows over-expression in squamous tumors and low expression in normal skin, breast and colon tissues. Notably, keratin and keratin-related genes have been extensively documented as potential markers for lung cancer including CYFRA2.1 (Pastor, A., et al, *Eur. Respir. J.*, 10:603-609, 1997). L513S (SEQ ID NO: 87 and 88)

shows moderate over-expression in several tumor tissues tested, and encodes a protein that was first isolated as a pemphigus vulgaris antigen.

L520S (SEQ ID NO: 95 and 96) and L521S (SEQ ID NO: 97 and 98) are highly expressed in lung squamous tumors, and L520S is up-regulated in normal salivary gland and L521S is over-expressed in normal skin. Both belong to a family of small proline rich proteins and represent markers for fully differentiated squamous cells. L521S has been described as a specific marker for lung squamous tumor (Hu, R., et al, *Lung Cancer*, 20:25-30, 1998). L515S (SEQ ID NO: 162) encodes IGF- β 2 and L516S is an aldose reductase homologue and both are moderately expressed in lung squamous tumors and in normal colon. Notably, L516S (SEQ ID NO: 91 and 92) is up-regulated in metastatic tumors but not primary lung adenocarcinoma, an indication of its potential role in metatasis and a potential prognostic marker. L522S (SEQ ID NO: 99) is moderately over-expressed in lung squamous tumors with minimum expression in normal tissues. L522S has been shown to belong to a class IV alcohol dehydrogenase, ADH7, and its expression profile suggests it is a squamous cell specific antigen. L523S (SEQ ID NO: 100) is moderately over-expressed in lung squamous tumor, human pancreatic cancer cell lines and pancreatic cancer tissues, suggesting this gene may be a shared antigen between pancreatic and lung squamous cell cancer.

L524S (SEQ ID NO: 101) is over-expressed in the majority of squamous tumors tested and is homologous with parathyroid hormone-related peptide (PTHrP), which is best known to cause humoral hypercalcaemia associated with malignant tumors such as leukemia, prostate and breast cancer. It is also believed that PTHrP is most commonly associated with squamous carcinoma of lung and rarely with lung adenocarcinoma (Davidson, L.A., et al, *J. Pathol.*, 178: 398-401, 1996). L528S (SEQ ID NO: 105) is highly over-expressed in two lung squamous tumors with moderate expression in two other squamous tumors, one lung adenocarcinoma and some normal tissues, including skin, lymph nodes, heart, stomach and lung. It encodes the NMB gene that is similar to the precursor of melanocyte specific gene Pmel17, which is reported to be preferentially expressed in low-metastatic potential melanoma cell lines. This suggests that L528S may be a shared antigen in both melanoma and lung squamous cell carcinoma. L526S (SEQ ID NO: 103) is overexpressed in all lung

squamous cell tumor tissues tested and has been shown to share homology with a gene (ATM) in which a mutation causes ataxia telangiectasia, a genetic disorder in humans causing a predisposition to cancer, among other symptoms. ATM encodes a protein that activates p53 mediated cell-cycle checkpoint through direct binding and phosphorylation of the p53 molecule. Approximately 40% of lung cancer is associated with p53 mutations, and it is speculated that over-expression of ATM is a result of compensation for loss of p53 function, but it is unknown whether over-expression is the cause of result of lung squamous cell carcinoma. Additionally, expression of L526S (ATM) is also detected in a metastatic but not lung adenocarcinoma, suggesting a role in metastasis.

Expression of L523S (SEQ ID NO: 175), was also examined by real time RT-PCR as described above. In a first study using a panel of lung squamous tumors, L523S was found to be expressed in 4/7 lung squamous tumors, 2/3 head and neck squamous tumors and 2/2 lung adenocarcinomas, with low level expression being observed in skeletal muscle, soft palate and tonsil. In a second study using a lung adenocarcinoma panel, expression of L523S was observed in 4/9 primary adenocarcinomas, 2/2 lung pleural effusions, 1/1 metastatic lung adenocarcinomas and 2/2 lung squamous tumors, with little expression being observed in normal tissues.

Expression of L523S in lung tumors and various normal tissues was also examined by Northern blot analysis, using standard techniques. In a first study, L523S was found to be expressed in a number of lung adenocarcinomas and squamous cell carcinomas, as well as normal tonsil. No expression was observed in normal lung. In a second study using a normal tissue blot (HB-12) from Clontech, no expression was observed in brain, skeletal muscle, colon, thymus, spleen, kidney, liver, small intestine, lung or PBMC, although there was strong expression in placenta.

EXAMPLE 3

ISOLATION AND CHARACTERIZATION OF LUNG TUMOR POLYPEPTIDES BY PCR-BASED SUBTRACTION

Eight hundred and fifty seven clones from a cDNA subtraction library, containing cDNA from a pool of two human lung squamous tumors subtracted against eight normal human tissue cDNAs including lung, PBMC, brain, heart, kidney, liver, pancreas, and skin, (Clontech, Palo Alto, CA) were derived and submitted to a first round of PCR amplification. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector P7- Adv vector (Clontech, Palo Alto, CA) and transformed into DH5 α *E. coli* (Gibco, BRL). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

One hundred and sixty two positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the the EMBL and GenBank databases, as described above, revealed no significant homologies to 13 of these clones, hereinafter referred to as Contigs 13, 16, 17, 19, 22, 24, 29, 47, 49, 56-59. The determined cDNA sequences for these clones are provided in SEQ ID NO: 125, 127-129, 131-133, 142, 144, 148-150, and 157, respectively. Contigs 1, 3-5, 7-10, 12, 11, 15, 20, 31, 33, 38, 39, 41, 43, 44, 45, 48, 50, 53, 54 (SEQ ID NO: 115-124, 126, 130, 134-141, 143, 145-147, respectively) were found to show some degree of homology to previously identified DNA sequences. Contig 57 (SEQ ID NO: 149) was found to represent the clone L519S (SEQ ID NO: 94) disclosed in US. Patent Application No. 09/123,912, filed July 27, 1998. To the best of the inventors' knowledge, none of these sequences have been previously shown to be differentially over-expressed in lung tumors.

mRNA expression levels for representative clones in lung tumor tissues, normal lung tissues (n=4), resting PBMC, salivary gland, heart, stomach, lymph nodes, skeletal muscle, soft palate, small intestine, large intestine, bronchial, bladder, tonsil, kidney, esophagus, bone marrow, colon, adrenal gland, pancreas, and skin, (all derived from human) were determined by RT-PCR as described above. Expression levels using microarray technology, as described above, were examined in one sample of each tissue type unless otherwise indicated.

Contig 3 (SEQ ID NO: 116) was found to be highly expressed in all head and neck squamous cell tumors tested (17/17), and expressed in the majority (8/12) of lung squamous tumors, (high expression in 7/12, moderate in 2/12, and low in 2/12), while showing negative expression for 2/4 normal lung tissues and low expression in the remaining two samples. Contig 3 showed moderate expression in skin and soft palate, and lowered expression levels in resting PBMC, large intestine, salivary gland, tonsil, pancreas, esophagus, and colon. Contig 11 (SEQ ID NO: 124) was found to be expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 14/17, and moderately expressed in 3/17. Additionally, expression in lung squamous tumors showed high expression in 3/12 and moderate in 4/12. Contig 11 was negative for 3/4 normal lung samples, with the remaining sample having only low expression. Contig 11 showed low to moderate reactivity to salivary gland, soft palate, bladder, tonsil, skin, esophagus, and large intestine. Contig 13 (SEQ ID NO: 125) was found to be expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 12/17, and moderately expressed in 5/17. Contig 13 was expressed in 7/12 lung squamous tumors, with high expression in 4/12 and moderate expression in three samples. Analysis of normal lung samples showed negative expression for 2/4 and low to moderate expression in the remaining two samples. Contig 13 did show low to moderate reactivity to resting PBMC, salivary gland, bladder, pancreas, tonsil, skin, esophagus, and large intestine, as well as high expression in soft palate. Contig 16 (SEQ ID NO: 127) was found to be moderately expressed in some head and neck squamous cell tumors (6/17) and one lung squamous tumor; while showing no expression in any normal lung samples tested. Contig 16 did show low reactivity to resting PBMC, large intestine, skin, salivary gland, and soft palate. Contig 17 (SEQ ID NO: 128) was shown to be expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 5/17, and moderately expressed in 12/17. Expression levels in lung squamous tumors showed one tumor sample with high expression and 3/12 with moderate levels. Contig 17 was negative for 2/4 normal lung samples, with the remaining samples having only low expression. Additionally, low level expression was found in esophagus and soft palate. Contig 19 (SEQ ID NO: 129) was found to be expressed in most head and neck squamous cell tumors tested (11/17); with two

samples having high levels, 6/17 showing moderate expression, and low expression being found in 3/17. Testing in lung squamous tumors revealed only moderate expression in 3/12 samples. Expression levels in 2/4 of normal lung samples were negative, the two other samples having only low expression. Contig 19 showed low expression levels in esophagus, resting PBMC, salivary gland, bladder, soft palate and pancreas.

Contig 22 (SEQ ID NO: 131), was shown to be expressed in most head and neck squamous cell tumors tested (13/17) with high expression in four of these samples, moderate expression in 6/17, and low expression in 3/17. Expression levels in lung squamous tumors were found to be moderate to high for 3/12 tissues tested, with negative expression in two normal lung samples and low expression in two other samples (n=4). Contig 22 showed low expression in skin, salivary gland and soft palate. Similarly, Contig 24 (SEQ ID NO: 132) was found to be expressed in most head and neck squamous cell tumors tested (13/17) with high expression in three of these samples, moderate expression in 6/17, and low expression in 4/17. Expression levels in lung squamous tumors were found to be moderate to high for 3/12 tissues tested, with negative expression for three normal lung samples and low expression in one sample (n=4). Contig 24 showed low expression in skin, salivary gland and soft palate. Contig 29 (SEQ ID NO: 133) was expressed in nearly all head and neck squamous cell tumors tested (16/17): highly expressed in 4/17, moderately expressed in 11/17, with low expression in one sample. Also, it was moderately expressed in 3/12 lung squamous tumors, while being negative for 2/4 normal lung samples. Contig 29 showed low to moderate expression in large intestine, skin, salivary gland, pancreas, tonsil, heart and soft palate. Contig 47 (SEQ ID NO: 142) was expressed in most head and neck squamous cell tumors tested (12/17): moderate expression in 10/17, and low expression in two samples. In lung squamous tumors, it was highly expressed in one sample and moderately expressed in two others (n=13). Contig 47 was negative for 2/4 normal lung samples, with the remaining two samples having moderate expression. Also, Contig 47 showed moderate expression in large intestine, and pancreas, and low expression in skin, salivary gland, soft palate, stomach, bladder, resting PBMC, and tonsil.

Contig 48 (SEQ ID NO: 143) was expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 8/17 and moderately expressed in 7/17, with low expression in two samples. Expression levels in lung squamous tumors were high to moderate in three samples (n=13). Contig 48 was negative for one out of four normal lung samples, the remaining showing low or moderate expression. Contig 48 showed moderate expression in soft palate, large intestine, pancreas, and bladder, and low expression in esophagus, salivary gland, resting PBMC, and heart. Contig 49 (SEQ ID NO: 144) was expressed at low to moderate levels in 6/17 head and neck squamous cell tumors tested. Expression levels in lung squamous tumors were moderate in three samples (n=13). Contig 49 was negative for 2/4 normal lung samples, the remaining samples showing low expression. Moderate expression levels in skin, salivary gland, large intestine, pancreas, bladder and resting PBMC were shown, as well as low expression in soft palate, lymph nodes, and tonsil. Contig 56 (SEQ ID NO: 148) was expressed in low to moderate levels in 3/17 head and neck squamous cell tumors tested, and in lung squamous tumors, showing low to moderate levels in three out of thirteen samples. Notably, low expression levels were detected in one adenocarcinoma lung tumor sample (n=2). Contig 56 was negative for 3/4 normal lung samples, and showed moderate expression levels in only large intestine, and low expression in salivary gland, soft palate, pancreas, bladder, and resting PBMC. Contig 58, also known as L769P, (SEQ ID NO: 150) was expressed at moderate levels in 11/17 head and neck squamous cell tumors tested and low expression in one additional sample. Expression in lung squamous tumors showed low to moderate levels in three out of thirteen samples. Contig 58 was negative for 3/4 normal lung samples, with one sample having low expression. Moderate expression levels in skin, large intestine, and resting PBMC were demonstrated, as well as low expression in salivary gland, soft palate, pancreas, and bladder. Contig 59 (SEQ ID NO: 157) was expressed in some head, neck, and lung squamous tumors. Low level expression of Contig 59 was also detected in salivary gland and large intestine.

The full-length cDNA sequence for Contig 22, also referred to as L763P, is provided in SEQ ID NO: 158, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 159. Real-time RT-PCR analysis of L763P revealed

that it is highly expressed in 3/4 lung squamous tumors as well as 4/4 head and neck squamous tumors, with low level expression being observed in normal brain, skin, soft pallet and trachea. Subsequent database searches revealed that the sequence of SEQ ID NO: 158 contains a mutation, resulting in a frameshift in the corresponding protein sequence. A second cDNA sequence for L763P is provided in SEQ ID NO: 345, with the corresponding amino acid sequence being provided in SEQ ID NO: 346. The sequences of SEQ ID NO: 159 and 346 are identical with the exception of the C-terminal 33 amino acids of SEQ ID NO: 159.

The full-length cDNA sequence incorporating Contigs 17, 19, and 24, referred to as L762P, is provided in SEQ ID NO: 160, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 161. Further analysis of L762P has determined it to be a type I membrane protein and two additional variants have been sequenced. Variant 1 (SEQ ID NO: 167, with the corresponding amino acid sequence in SEQ ID NO: 169) is an alternatively spliced form of SEQ ID NO: 160 resulting in deletion of 503 nucleotides, as well as deletion of a short segment of the expressed protein. Variant 2 (SEQ ID NO: 168, with the corresponding amino acid sequence in SEQ ID NO: 170) has a two nucleotide deletion at the 3' coding region in comparison to SEQ ID NO: 160, resulting in a secreted form of the expressed protein. Real-time RT-PCR analysis of L762P revealed that is over-expressed in 3/4 lung squamous tumors and 4/4 head & neck tumors, with low level expression being observed in normal skin, soft pallet and trachea.

The full-length cDNA sequence for contig 56 (SEQ ID NO: 148), also referred to as L773P, is provided in SEQ ID NO: 171, with the predicted amino acid sequence in SEQ ID NO: 172. L773P was found to be identical to dihydroxyl dehydrogenase at the 3' portion of the gene, with divergent 5' sequence. As a result, the 69 N-terminal amino acids are unique. The cDNA sequence encoding the 69 N-terminal amino acids is provided in SEQ ID NO: 349, with the N-terminal amino acid sequence being provided in SEQ ID NO: 350. Real-time PCR revealed that L773P is highly expressed in lung squamous tumor and lung adenocarcinoma, with no detectable expression in normal tissues. Subsequent Northern blot analysis of L773P demonstrated that this transcript is differentially over-expressed in squamous tumors

and detected at approximately 1.6 Kb in primary lung tumor tissue and approximately 1.3 Kb in primary head and neck tumor tissue.

Subsequent microarray analysis has shown Contig 58, also referred to as L769S (SEQ ID NO: 150), to be overexpressed in breast tumors in addition to lung squamous tumors.

EXAMPLE 4

SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems Division 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

EXAMPLE 5

PREPARATION OF ANTIBODIES AGAINST LUNG CANCER ANTIGENS

Polyclonal antibodies against the lung cancer antigens L514S, L528S and L531S (SEQ ID NO: 155, 225 and 112, respectively) were prepared as follows.

Rabbits were immunized with recombinant protein expressed in and purified from *E. coli* as described above. For the initial immunization, 400 µg of

antigen combined with muramyl dipeptide (MDP) was injected subcutaneously (S.C.). Animals were boosted S.C. 4 weeks later with 200 µg of antigen mixed with incomplete Freund's Adjuvant (IFA). Subsequent boosts of 100 µg of antigen mixed with IFA were injected S.C. as necessary to induce high antibody titer responses. Serum bleeds from immunized rabbits were tested for antigen-specific reactivity using ELISA assays with purified protein. Polyclonal antibodies against L514S, L528S and L531S were affinity purified from high titer polyclonal sera using purified protein attached to a solid support.

Immunohistochemical analysis using polyclonal antibodies against L514S was performed on a panel of 5 lung tumor samples, 5 normal lung tissue samples and normal colon, kidney, liver, brain and bone marrow. Specifically, tissue samples were fixed in formalin solution for 24 hours and embedded in paraffin before being sliced into 10 micron sections. Tissue sections were permeabilized and incubated with antibody for 1 hr. HRP-labeled anti-mouse followed by incubation with DAB chromogen was used to visualize L514S immunoreactivity. L514S was found to be highly expressed in lung tumor tissue with little or no expression being observed in normal lung, brain or bone marrow. Light staining was observed in colon and kidney. Staining was seen in normal liver but no mRNA has been detected in this tissue making this result suspect.

EXAMPLE 6

PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

Immunogenic peptides from the lung cancer antigen L762P (SEQ ID NO: 161) for HLA-A2/K^b-restricted CD8⁺ T cells were identified as follows.

The location of HLA-A2 binding peptides within the lung cancer antigen L762P (SEQ ID NO: 161) was predicted using a computer program which predicts peptides sequences likely to be to HLA-A*0201 by fitting to the known peptide binding motif for HLA-A*0201 (Rupert *et al.* (1993) *Cell* 74:929; Rammensee *et al.* (1995) *Immunogenetics* 41:178-228). A series of 19 synthetic peptides corresponding to a selected subset of the predicted HLA-A*0201 binding peptides was prepared as described above.

Mice expressing the transgene for human HLA A2/K^b (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with the synthetic peptides, as described by Theobald et al., *Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995 with the following modifications. Mice were immunized with 50µg of L726P peptide and 120µg of an I-A^b binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell suspensions prepared. Cells were then resuspended at 7×10^6 cells/ml in complete media (RPMI-1640; Gibco BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL), 2×10^{-5} M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) L762P peptide- (5µg/ml) and 10mg/ml B₂-microglobulin- (3 µg/ml) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). After six days, cells (5×10^5 /ml) were restimulated with 2.5×10^6 /ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells (Sherman et al, *Science* 258:815-818, 1992) and 5×10^6 /ml irradiated (3000 rads) A2/K^b-transgenic spleen feeder cells. Cells were cultured in the presence of 10U/ml IL-2. Cells were restimulated on a weekly basis as described, in preparation for cloning the line.

Peptide-specific cell lines were cloned by limiting dilution analysis with irradiated (20,000 rads) L762P peptide-pulsed EL4 A2Kb tumor cells (1×10^4 cells/well) as stimulators and irradiated (3000 rads) A2/K^b-transgenic spleen cells as feeders (5×10^5 cells/ well) grown in the presence of 10U/ml IL-2. On day 7, cells were restimulated as before. On day 14, clones that were growing were isolated and maintained in culture.

Cell lines specific for L762P-87 (SEQ ID NO: 226; corresponding to amino acids 87-95 of SEQ ID NO: 161), L726P-145 (SEQ ID NO: 227; corresponding to amino acids 145-153 of SEQ ID NO: 161), L726P-585 (SEQ ID NO: 228; corresponding to amino acids 585-593 of SEQ ID NO: 161), L762P-425 (SEQ ID NO: 229; corresponding to amino acids 425-433 of SEQ ID NO: 161), L762P(10)-424 (SEQ ID NO: 230; corresponding to amino acids 424-433 of SEQ ID NO: 161) and L762P(10)-458 (SEQ ID NO: 231; corresponding to amino acids 458-467 of SEQ ID

NO: 161) demonstrated significantly higher reactivity (as measured by percent specific lysis) against L762P peptide-pulsed EL4-A2/K^b tumor target cells than control peptide-pulsed EL4-A2/K^b tumor target cells.

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EXAMPLE 7

IDENTIFICATION OF CD4 IMMUNOGENIC T CELL EPITOPES DERIVED
FROM THE LUNG CANCER ANTIGEN L762P

CD4 T cell lines specific for the antigen L762P (SEQ ID NO: 161) were
10 generated as follows.

A series of 28 overlapping peptides were synthesized that spanned approximately 50% of the L762P sequence. For priming, peptides were combined into pools of 4-5 peptides, pulsed at 20 micrograms/ml into dendritic cells for 24 hours. The dendritic cells were then washed and mixed with positively selected CD4⁺ T cells in 96
15 well U-bottomed plates. Forty cultures were generated for each peptide pool. Cultures were restimulated weekly with fresh dendritic cells loaded with peptide pools. Following a total of 3 stimulation cycles, cells were rested for an additional week and tested for specificity to antigen presenting cells (APC) pulsed with peptide pools using interferon-gamma ELISA and proliferation assays. For these assays, adherent
20 monocytes loaded with either the relevant peptide pool or an irrelevant peptide were used as APC. T cell lines that appeared to specifically recognize L762P peptide pools both by cytokine release and proliferation were identified for each pool. Emphasis was placed on identifying T cells with proliferative responses. T cell lines that demonstrated either both L762P-specific cytokine secretion and proliferation, or strong proliferation
25 alone were further expanded to be tested for recognition of individual peptides from the pools, as well as for recognition of recombinant L762P. The source of recombinant L762P was *E. coli*, and the material was partially purified and endotoxin positive. These studies employed 10 micrograms of individual peptides, 10 or 2 micrograms of an irrelevant peptide, and 2 or 0.5 micrograms of either L762P protein or an irrelevant,
30 equally impure, *E. coli* generated recombinant protein. Significant interferon-gamma production and CD4 T cell proliferation was induced by a number of L762P-derived

peptides in each pool. The amino acid sequences for these peptides are provided in SEQ ID NO: 232-251. These peptides correspond to amino acids 661-680, 676-696, 526-545, 874-893, 811-830, 871-891, 856-875, 826-845, 795-815, 736-755, 706-725, 706-725, 691-710, 601-620, 571-590, 556-575, 616-635, 646-665, 631-650, 541-560 and 586-605, respectively, of SEQ ID NO: 161.

CD4 T cell lines that demonstrated specificity for individual L762P-derived peptides were further expanded by stimulation with the relevant peptide at 10 micrograms/ml. Two weeks post-stimulation, T cell lines were tested using both proliferation and IFN-gamma ELISA assays for recognition of the specific peptide. A number of previously identified T cells continued to demonstrate L762P-peptide specific activity. Each of these lines was further expanded on the relevant peptide and, following two weeks of expansion, tested for specific recognition of the L762P-peptide in titration experiments, as well as for recognition of recombinant *E. coli*-derived L762P protein. For these experiments, autologous adherent monocytes were pulsed with either the relevant L762P-derived peptide, an irrelevant mammaglobin-derived peptide, recombinant *E. coli*-derived L762P (approx. 50% pure), or an irrelevant *E. coli*-derived protein. The majority of T cell lines were found to show low affinity for the relevant peptide, since specific proliferation and IFN-gamma ratios dramatically decreased as L762P peptide was diluted. However, four lines were identified that demonstrated significant activity even at 0.1 micrograms/ml peptide. Each of these lines (referred to as A/D5, D/F5, E/A7 and E/B6) also appeared to specifically proliferate in response to the *E. coli*-derived L762P protein preparation, but not in response to the irrelevant protein preparation. The amino acid sequences of the L762P-derived peptides recognized by these lines are provided in SEQ ID NO: 234, 249, 236 and 245, respectively. No protein specific IFN-gamma was detected for any of the lines. Lines A/D5, E/A7 and E/B6 were cloned on autologous adherent monocytes pulsed with the relevant peptide at 0.1 (A/D5 and E/A7) or 1 (D/F5) microgram/ml. Following growth, clones were tested for specificity for the relevant peptide. Numerous clones specific for the relevant peptide were identified for lines A/D5 and E/A7.

EXAMPLE 8**PROTEIN EXPRESSION OF LUNG TUMOR-SPECIFIC ANTIGENS****5 a) Expression of L514S in *E. coli***

The lung tumor antigen L514S (SEQ ID NO: 89) was subcloned into the expression vector pE32b at NcoI and NotI sites, and transformed into *E. coli* using standard techniques. The protein was expressed from residues 3-153 of SEQ ID NO: 89. The expressed amino acid sequence and the corresponding DNA sequence are
10 provided in SEQ ID NO: 252 and 253, respectively.

b) Expression of L762P

Amino acids 32-944 of the lung tumor antigen L762P (SEQ ID NO: 161), with a 6X His Tag, were subcloned into a modified pET28 expression vector,
15 using kanamycin resistance, and transformed into BL21 CodonPlus using standard techniques. Low to moderate levels of expression were observed. The determined DNA sequence of the L762P expression construct is provided in SEQ ID NO: 254.

From the foregoing it will be appreciated that, although specific
20 embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

CLAIMS

1. An isolated polypeptide, comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a) sequences recited in SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 under moderately stringent conditions; and

(c) complements of sequences of (a) or (b).

2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158,

160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 or a complement of any of the foregoing polynucleotide sequences.

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3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NO: 110, 112, 114, 152, 155, 156, 159, 161, 165, 166, 169, 170, 172, 174, 176, 226-252, 346, 348 and 350.

4. An isolated polynucleotide encoding at least 15 amino acid residues of a lung tumor protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 or a complement of any of the foregoing sequences.

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5. An isolated polynucleotide encoding a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 or a complement of any of the foregoing sequences.

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6. An isolated polynucleotide, comprising a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349.

7. An isolated polynucleotide, comprising a sequence that hybridizes to a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 under moderately stringent conditions.

8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.

9. An expression vector, comprising a polynucleotide according to any one of claims claim 4-8.

10. A host cell transformed or transfected with an expression vector according to claim 9.

11. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a lung tumor protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84,

86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and
5 349 or a complement of any of the foregoing polynucleotide sequences.

12. A fusion protein, comprising at least one polypeptide according to claim 1.

10 13. A fusion protein according to claim 12, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.

14. A fusion protein according to claim 12, wherein the fusion
15 protein comprises a T helper epitope that is not present within the polypeptide of claim 1.

15. A fusion protein according to claim 12, wherein the fusion protein comprises an affinity tag.

20

16. An isolated polynucleotide encoding a fusion protein according to claim 12.

17. A pharmaceutical composition, comprising a physiologically
25 acceptable carrier and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to claim 11;
- (d) a fusion protein according to claim 12; and
- 30 (e) a polynucleotide according to claim 16.

18. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:
- (a) a polypeptide according to claim 1;
 - (b) a polynucleotide according to claim 4;
 - (c) an antibody according to claim 11;
 - (d) a fusion protein according to claim 12; and
 - (e) a polynucleotide according to claim 16.
19. A vaccine according to claim 18, wherein the immunostimulant is an adjuvant.
20. A vaccine according to any claim 18, wherein the immunostimulant induces a predominantly Type I response.
21. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 17.
22. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 18.
23. A pharmaceutical composition comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.
24. A pharmaceutical composition according to claim 23, wherein the antigen presenting cell is a dendritic cell or a macrophage.

25. A vaccine comprising an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

5 (a) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171,
10 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions;
and

(c) complements of sequences of (i) or (ii);

in combination with an immunostimulant.

15 26. A vaccine according to claim 25, wherein the immunostimulant is an adjuvant.

27. A vaccine according to claim 25, wherein the immunostimulant induces a predominantly Type I response.

20 28. A vaccine according to claim 25, wherein the antigen-presenting cell is a dendritic cell.

29. A method for inhibiting the development of a cancer in a patient,
25 comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

30 (a) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and

349;

- (b) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions; and
- (c) complements of sequences of (i) or (ii) encoded by a polynucleotide recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349; and thereby inhibiting the development of a cancer in the patient.

30. A method according to claim 29, wherein the antigen-presenting cell is a dendritic cell.

31. A method according to any one of claims 21, 22 and 29, wherein the cancer is lung cancer.

32. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349; and

(ii) complements of the foregoing polynucleotides;

wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the antigen from the sample.

33. A method according to claim 32, wherein the biological sample is blood or a fraction thereof.

34. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 32.

35. A method for stimulating and/or expanding T cells specific for a lung tumor protein, comprising contacting T cells with at least one component selected from the group consisting of:

(a) polypeptides comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349;

(ii) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions; and

(iii) complements of sequences of (i) or (ii);

(b) polynucleotides encoding a polypeptide of (a); and

(c) antigen presenting cells that express a polypeptide of (a);

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

36. An isolated T cell population, comprising T cells prepared according to the method of claim 35.

37. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 36.

38. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of:

(i) polypeptides comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

10 (1) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349;

(2) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions; and

(3) complements of sequences of (1) or (2);

(ii) polynucleotides encoding a polypeptide of (i); and

(iii) antigen presenting cells that expresses a polypeptide of (i);

20 such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

39. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of:

(i) polypeptides comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence

selected from the group consisting of:

- (1) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349;
- 5 (2) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions; and
- (3) complements of sequences of (1) or (2);
- 10 (ii) polynucleotides encoding a polypeptide of (i); and
- (iii) antigen presenting cells that express a polypeptide of (i); such that T cells proliferate;
- (b) cloning at least one proliferated cell to provide cloned T cells; and
- 15 (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

40. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

- 20 (a) contacting a biological sample obtained from a patient with a binding agent that binds to a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 or a complement of any of the
- 25 foregoing polynucleotide sequences;
- (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and
- (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

41. A method according to claim 40, wherein the binding agent is an

antibody.

42. A method according to claim 43, wherein the antibody is a monoclonal antibody.

5 43. A method according to claim 40, wherein the cancer is lung cancer.

44. A method for monitoring the progression of a cancer in a patient,
10 comprising the steps of:

(a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160,
15 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent;

(c) repeating steps (a) and (b) using a biological sample obtained
20 from the patient at a subsequent point in time; and

(d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

25 45. A method according to claim 44, wherein the binding agent is an antibody.

46. A method according to claim 45, wherein the antibody is a monoclonal antibody.

30 47. A method according to claim 44, wherein the cancer is a lung

cancer.

48. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

- 5 (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347
10 and 349 or a complement of any of the foregoing polynucleotide sequences;
- (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and
- (c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the
15 presence or absence of a cancer in the patient.

49. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

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50. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

25

51. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

- (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a
30 polynucleotide sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347

and 349 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

10 52. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

15 53. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

54. A diagnostic kit, comprising:

(a) one or more antibodies according to claim 11; and

20 (b) a detection reagent comprising a reporter group.

55. A kit according to claim 54, wherein the antibodies are immobilized on a solid support.

25 56. A kit according to claim 54, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

30 57. A kit according to claim 54, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.

58. An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 or a complement of any of the foregoing polynucleotides.

59. A oligonucleotide according to claim 58, wherein the oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349.

20

60. A diagnostic kit, comprising:

- (a) an oligonucleotide according to claim 59; and
- (b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

25

SEQUENCE LISTING

<110> Corixa Corporation et al.

<120> COMPOUNDS AND METHODS FOR THERAPY
AND DIAGNOSIS OF LUNG CANCER

<130> 210121.45501PC

<140> PCT

<141> 2000-04-03

<160> 350

<170> FastSEQ for Windows Version 3.0

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<212> DNA

<213> Homo sapien

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ttcatctcca gcagagacaa cggaggaggc tcccaccagg acggttctca ttatttatat	180
gttaatatgt ttgtaaactc atgtacagtt ttttttgggg gggaagcaat gggaanggta	240
naaattacaa atagaatcat ttgctgtaat ccttaaatgg caaacgggtca ggccacgtga	300
aaaaaaaaaa aaaaa	315

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<212> DNA

<213> Homo sapien

<400> 2

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atatatataa acaaatacaa aaagttttga gtggttcagc ttttttattt tttttaatgg	120
cataactttt aacaacactg ctctgtaatg ggttgaactg tggtaactcag actgagataa	180
ctgaaatgag tggatgtata gtgttattgc ataattatcc cactatgaag caaagggact	240
ggataaaattc ccagctctaga ttattagcct ttgttaacca tcaagcacct agaagaagaa	300
ttattggaaa ttttgcctc tgtaactggc actttggggg gtgacttatc ttttgccttt	360
gtaaaaaaaa aaaaaaaaaa	380

<210> 3

<211> 346

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<220>
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 <222> (1)...(346)
 <223> n = A,T,C or G

<400> 3
 ttgtaagtat acaatttttag aaaggattaa atgttattga tcattttact gaatactgca 60
 catcctcacc atacaccatc cactttccaa taacatttaa tcctttctaa aattgtâagt 120
 atacaattgt actttctttg gattttcata acaaatatac catagactgt taattttatt 180
 gaagtttctt taatggaatg agtcattttt gtcttgtgct tttgaggta cctttgcttt 240
 gacttccaac aatttgatca tatagtgttg agctgtggaa atctttaagt ttattctata 300
 gcaataattt ctattnnnag annccngggn naaaannann annaaa 346

<210> 4
 <211> 372
 <212> DNA
 <213> Homo sapien

<220>
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 <222> (1)...(372)
 <223> n = A,T,C or G

<400> 4
 actagtctca ttactccaga attatgctct tgtacctgtg tggctggggt tcttagtctg 60
 tggtttggtt tggttttttg aactggtatg taggggtggt cacagtctca atgtaagcac 120
 tcctttctcc aagtgtgct ttgtggggac aatcattctt tgaacattag agaggaaggc 180
 agttcaagct gttgaaaaga ctattgctta tttttgtttt taaagaccta cttgacgtca 240
 tgtggacagt gcacgtgcct tacgtacat cttgttttct aggaagaagg ggatgcnggg 300
 aaggantggg tgctttgtga tggataaaac gnctaaataa cacaccttta cattttgaaa 360
 aaaacaaaac aa 372

<210> 5
 <211> 698
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(698)
 <223> n = A,T,C or G

<400> 5
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 cctaaccag gtttaactgca agaagaggcg ggatactttc agctttccat gtaactgtat 120
 gcataaagcc aatgtagtcc agtttctaag atcatgttcc aagctaactg aatcccactt 180
 caatacacac tcatgaactc ctgatggaac aataacaggc ccaagcctgt ggtatgatgt 240
 gcacacttgc tagactcaga aaaaatacta ctctcataaa tgggtgggag tattttgggt 300
 gacaacctac tttgcttggc tgagtgaagg aatgatattc atatnttcac ttattccatg 360
 gacatttagt tagtgctttt tatataccag gcatgatgct gagtgacact cttgtgtata 420
 tntccaaatn ttngtnngt cgctgcacat atctgaaac ctatattaag antttcccaa 480
 natgangtcc ctggtttttc cacgccactt gatcngtcaa ngatctcacc tctgtntgtc 540
 ctaaaacnt ctncnnang gttagacngg acctctcttc tcccttcccg aanaatnaag 600
 tgtgngaaga nancncnch cccccctnch tncnncctng ccngctnnnc cncntgtngg 660

gggngccgcc cccgcggggg gacccccccn ttttcccc

698

<210> 6
 <211> 740
 <212> DNA
 <213> Homo sapien

 <220>
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 <222> (1)...(740)
 <223> n = A,T,C or G

<400> 6
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 catgtttatc ttttattatg tnttgtgaag ttgtgtcttt tcaactaatta cctatactat 120
 gccaatattt ccttatatct atccataaca tttatactac atttgtaaga gaatatgcac 180
 gtgaaactta acactttata aggtaaaaat gaggtttcca agatttaata atctgatcaa 240
 gttcttggtta tttccaaata gaatggactt ggtctgttaa ggggctaagg gagaagaaga 300
 agataagggtt aaaagtgtgtt aatgacccaaa cattctaaaa gaaatgcaaa aaaaaattta 360
 ttttcaagcc ttcgaactat ttaaggaaag caaatcatt tcctanatgc atatcatttg 420
 tgagantttc tcantaatat cctgaatcat tcatttcagc tnaggcttca tgttgactcg 480
 atatgtcatc tagggaaagt ctatttcagc gtccaaacct gttgccatag ttggttaggc 540
 tttcctttaa ntgtgaanta ttnacangaa attttctctt tnanagttct tnatagggtt 600
 aggggtgtgg gaaaagcttc taacaatctg tagtgttncg tggtatctgt ncagaaccan 660
 aatnacggat cgnangaagg actgggtcta tttacangaa cgaatnatct ngttmmtgt 720
 gtnnncaact ccngggagcc 740

<210> 7
 <211> 670
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(670)
 <223> n = A,T,C or G

<400> 7
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 agcgcccccg gctcgatggc cccgtggtgc tcagttagca gcggccccgc gcgctacgtg 120
 cttgggatgc aggagctgtt ccggggccac agcaagaccg cgagttcctg gcgcacagcg 180
 ccaaggtgca ctcggtggcc tggagttgag acgggctgct cctacctcgg ggtcttcgac 240
 aagacgccac gtcttcttgc tgganaanga ccgttggtca aagaaaacaa ttatcgggga 300
 catggggata gtgtggacca ctttgttggc atccaagtaa tcctgacctt tttgttacgg 360
 cgtctggaga taaaaccatt cgcattctgg atgtgaggac tacaaaatgc attgccactg 420
 tgaactacta aggggagaac attaatatct gctggantcc tgatgggcan accattgctg 480
 tagcnacaag gatgatgtgg tgactttatt gatgccaaag aacccccgtt caaagcaaaa 540
 aaacanttcc aanttccaag tcaccnaaat ctcttggaac aatgaacatn aatatnttct 600
 tcctgacaat ggnccctggg tgnntcacat cctcagctnc cccaaaactg aancctgtnc 660
 natccacccc 670

<210> 8
 <211> 689
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (689)
 <223> n = A,T,C or G

<400> 8
 actagtatct aggaatgaac agtaaaagag gagcagttgg ctacttgatt acaacagagt 60
 aaatgaagta ctggatttgg gaaaacctgg ttttattaga acatatggaa tgaaagccta 120
 cacctagcat tgcctactta gcccctgaa ttaacagagc ccaattgaga caaacccctg 180
 gcaacaggaa attcaaggga gaaaaagtaa gcaacttggg ctaggatgag ctgactccct 240
 tagagcaaag ganagacagc ccccattacc aaataccatt ttgacctggg gcttgtgcag 300
 ctggcagtggt tcctgccccca gcatggcacc ttatngtttt gatagcaact tcgttgaatt 360
 ttcaccaact tattacttga aattataata tagcctgtcc gtttgcgtgn tccaggctgt 420
 gatatatntt cctagtgggt tgactttnaa aataaatnag gtttantttt cccccccnn 480
 cnnctnctncc nntcnctcnn cnnccccccc cncctngtcc tccnnnnnttn gggggggccn 540
 cccccnogggn ggacccccct ttggtccctt agtggagggt natggccccct ggnnttatcc 600
 nggcctann tttccccgtn mnaaatgntt cccctccca ntccnccac ctcaanccgg 660
 aagcctaagt ttntaccctg ggggtcccc 689

<210> 9
 <211> 674
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (674)
 <223> n = A,T,C or G

<400> 9
 gtccactctc ctttgagtgt actgtcttac tgtgcactct gtttttcaac tttctagata 60
 taataaatgc ttgttctata gtggagtaag agctcacaca cccaaggcag caagataact 120
 gaaaaaagcg aggctttttt gccaccttgg taaaggccag ttcactgcta tagaactgct 180
 ataagcctga agggaagtag ctatgagact ttccattttt cttagtctc ccaataggct 240
 ccttcatgga aaaaggcttc ctgtaataat tttcacctaa tgaattagca gtgtgattat 300
 ttctgaaata agagacaaat tgggcgcag agtcttctctg tgatttaaaa taacaaccc 360
 aaagttttgt ttggtcttca ccaaaggaca tactctaggg ggtatgttgt tgaagacatt 420
 caaaaacatt agctgttctg tctttcaatt tcaagttatt ttggagactg cctccatgtg 480
 agttaattac tttgctctgg aactagcatt attgtcatta tcatcacatt ctgtcatcat 540
 catctgaata atattgtgga tttccccctc tgcttgcatc ttcttttgac tctctggga 600
 anaaatgtca aaaaaaagg tcgatctact cngcaaggnc catctaataca ctgcgctgga 660
 aggaccnct gcc 674

<210> 10
 <211> 346
 <212> DNA
 <213> Homo sapien

<220>
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 <222> (1) ... (346)
 <223> n = A,T,C or G

<400> 10

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ttctgtctgt	aacaaaaatg	tactttatag	agatggagga	aaaggtctaa	tactacatag	120
ccttaagtgt	ttctgtcatt	gttcaagtgt	atcttctgta	acagaaacat	atttggaatg	180
tttttctttt	ccccttataa	attgtaattc	ctgaaatact	gctgctttta	aaagtcacc	240
tgtcagatta	tattatctaa	caattgaata	ttgtaaata	acttgtctta	cctctcaata	300
aaaggtact	tttctattan	nnagnngnnn	gnnnnataaa	anaaaa		346

<210> 11

<211> 602

<212> DNA

<213> Homo sapien

<400> 11

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gatgttaagc	tttttgaaaa	gtttagggtta	aacctactgt	tgtagatta	atgtatttgt	120
tgcttccctt	tatctggaat	gtggcattag	cttttttatt	ttaaccctct	ttaattotta	180
ttcaattcca	tgacttaagg	ttggagagct	aaacactggg	atctttggat	aacagactga	240
cagttttgca	taattataat	cggcattgta	catagaaagg	atatggctac	cttttggtta	300
atctgcactt	tctaaatata	aaaaaaggga	aatgaagtta	taaatcaatt	tttgataat	360
ctgtttgaaa	catgagtttt	atttgcttaa	tattagggtc	ttgccccttt	tctgtaagtc	420
tcttgggata	ctgtgtagaa	ctgttctcat	taaacaccaa	acagttaagt	ccattctctg	480
gtactagcta	caaattcggg	ttcatattct	acttaacaat	ttaaataaac	tgaaatattt	540
ctagatgggtc	tacttctgtt	catataaaaa	caaaacttga	tttccaaaaa	aaaaaaaaaa	600
aa						602

<210> 12

<211> 685

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(685)

<223> n = A,T,C or G

<400> 12

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gcatgcattt	gtaacatgat	tagtagattt	gaatatatag	atgtagtatn	ttgggtatct	180
aggtgtttta	tcattatgta	aaggaattaa	agtaaaggac	ttttagtttg	tttttattaa	240
atatgcatat	agtagagtgc	aaaaatatag	caaaaatana	aactaaagg	agaaaagcat	300
tttagatatg	ccttaatnta	nnaactgtgc	caggtggccc	tcggaataga	tgccaggcag	360
agaccagtgc	ctgggtggtg	cctccccttg	tctgcccccc	tgaagaactt	ccctcacgtg	420
angtagtgcc	ctcgtagggtg	tcacgtggan	tantgggganc	aggccgnnncn	gtnanaagaa	480
ancanngtga	nagtttcncc	gtngangcng	aactgtccct	gngccnnnac	gctcccanaa	540
cntntccaat	ngacaatcga	gtttccnnnc	tcengnaacc	tngccgnnnn	cnngcccnnc	600
cantntgnta	accccgcgcc	cggatcgctc	tcnnntcggt	ctcncncnaa	ngggntttcn	660
cnnccgcggt	cncnnccccg	cnncc				685

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<211> 694

<212> DNA

<213> Homo sapien

<220>

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 <222> (1) ... (694)
 <223> n = A,T,C or G

<400> 13

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cagaataaatt	ttataaaatg	ttttagagtt	ataattgccg	aaaataattt	aaagacactt	180
tttctctgtg	tgtgcaaagt	tgtgtttgtg	atccattttt	tttttttttt	taggacacct	240
gtttactagc	tagctttaca	atatgccaaa	aaaggatttc	tccttgacct	catcogtggt	300
tcacctcttt	ttccccccat	gctttttgcc	ctagtttata	acaaagggaat	gatgatgatt	360
taaaaagtag	ttctgtatct	tcagtatctt	ggtcttccag	aacctctctg	ttgggaagg	420
gatcattttt	tactggtcat	ttccctttgg	agtgtactac	tttaacagat	ggaaagaact	480
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ctggcntgat	tggctctggc	gccgtcattg	tcagcacagt	gccatgggac	atggggaana	600
ctgactgcac	ngccaatgg	tttcatgaag	aatacngcat	ncncngtgat	cacgtnancc	660
angacgctat	gggggncana	gggcccantg	cttc			694

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 <211> 679
 <212> DNA
 <213> Homo sapien

<220>
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 <222> (1) ... (679)
 <223> n = A,T,C or G

<400> 14

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agtcgcgnac	cgttccggcc	cangctnagt	tagnctcac	catnccggte	aaaggangca	120
ccaagtgcac	caaatacctg	cngtnccgat	ntaaattcat	cttctggctt	gccgggattg	180
ctgtccntgc	cattggacta	nggctccgat	ncgactctca	gaccanganc	atcttcganc	240
naganactaa	tnatnattnt	tcagcttct	acacaggagt	ctatattctg	atcggatccg	300
gcncctcnt	gatgctggtg	ggcttcctga	gctgctgagg	ggctgtgcaa	gagtcctant	360
gcatgctggg	actgttcttc	ggcttcntct	tggtgatatn	cgccattgaa	atacctgcgg	420
ccatctgggg	atattccact	ncgatnatgt	gattaaggaa	ntccacggag	ttttacaagg	480
acacgtacaa	cnacctgaaa	accnnggatg	anccccaccg	ggaancnctg	aangccatcc	540
actatgcgtt	gaactgcaat	ggtttggctg	gggnccttga	acaatttaac	cncatacatc	600
tggccccann	aaaggacntn	ctcganncc	tcnccgtgna	attcngttct	gatnccatca	660
cagaagtctc	gaacaatcc					679

<210> 15
 <211> 695
 <212> DNA
 <213> Homo sapien

<220>
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 <222> (1) ... (695)
 <223> n = A,T,C or G

<400> 15

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cattacaact	acccaatccg	aagtgtcaac	tgtgtcagga	ctaanaaacc	ctggttttga	120

ttaaaaaagg	gcctgaaaaa	aggggagcca	caaactctgtc	tgcttcctca	cnttantcnt	180
tggcaaatna	gcattctgtc	tcnttggtcg	cngcctcanc	ncaaaaaanc	ngaactcnat	240
cnggcccagg	aatacatctc	ncaatnaacn	aaattganca	aggcnntggg	aaatgccnga	300
tgggattatc	ntccgcttgt	tganccttcta	agtttcnttc	ccttcattcn	accctgccag	360
ccnagttctg	ttagaaaaat	gccngaattc	naacnccggg	tttctactc	ngaatttaga	420
ttcncanaaa	cttcttggtc	acnattcnaa	ttnanggnca	cgnacanatn	ccttccatna	480
ancncacccc	acntttgana	gccangacaa	tgactgcntn	aantgaaggc	ntgaaggaaan	540
aaactttgaaa	ggaaaaaaa	ctttgtttcc	ggcccttcc	aacncttctg	tgtttnancac	600
tgccctctng	naaccctgga	agcccnngga	cagtgttaca	tggtgttcta	nnaaacngac	660
ncttnaatnt	cnatcttccc	nanaacgatt	ncncc			695

<210> 16

<211> 669

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(669)

<223> n = A,T,C or G

<400> 16

cgccgaagca	gcagcgagg	ttgtccccgt	tccccctccc	ccttcccttc	tcgggttgcc	60
ttcccgggcc	ccttacactc	cacagtcccg	gtcccgccat	gtcccagaaa	caagaagaag	120
agaaccctgc	ggaggagacc	ggcgaggaga	agcaggacac	gcaggagaaa	gaaggtattc	180
tgccctgagag	agctgaagag	gcaaagctaa	aggccaaata	cccaagccta	ggacaaaagc	240
ctggaggctc	cgacttcctc	atgaagagac	tccagaaagg	gcaaaaagta	tttgactcng	300
gagactacaa	catggccaaa	gccaacatga	agaataagca	gctgcccaagt	gcangaccag	360
acaagaacct	ggtgactggt	gatcacatcc	ccaccccaca	ggatctgccc	agagaaagtc	420
ctcgtctgtc	accagcaagc	ttgcggtggt	ccaagttgaa	tgatctgccc	ggggctctgc	480
canatctgag	acgtttccct	ccctgcccc	cccggttctt	gtgctggctc	ctgcccttcc	540
tgcttttgca	gccanggggc	aggaagtggc	ncnggtngtg	gctggaaagc	aaaacccttt	600
cctgttggtg	tcccacccat	ggagccccctg	ggcgagccc	angaacttga	ncctttttgt	660
tnctttncc						669

<210> 17

<211> 697

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(697)

<223> n = A,T,C or G

<400> 17

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gacgcgtgta	ggagannnac	gctggcccan	ctgcgggcca	cacacgggga	tcntggtnat	120
gcctgcccnn	gggancccca	ncnctcggan	cccatntcac	acccgnnccn	tnccgcccacn	180
ncctggctcn	cncngcccng	nccagctcnc	gnccccctcc	gccnnnctcn	ttnnctctc	240
cncnccctcc	ncnacnac	cctaccncg	gtccctccc	cagccccccc	ccgcaancct	300
ccacnacncc	ntennncga	ancnccnctc	gnctcngcc	ccngccccct	gccccccgcc	360
cncnacnncc	cgntcccccg	cgncngcngc	ctnccccct	cccacnacag	ncncacccgc	420
agncaagcnc	tccgcccnc	gacgcccnn	cccgccgcgc	tcaccttc	ggnccnacng	480
ccccgctcnc	ncnctgcnc	gccngcnngg	cgcgccgcc	cnnccngntn	ccnccngng	540

```

ccccngcngn angcngtgcg cnncaangncc gngccggnncn ncaccctccg nccnccgccc 600
cgcccgctgg gggctcccgc cncgcggncc antcccccnc cntnccgcca ctntccgntc 660
cnnctctcnc gctcngcgcn cgcccnccnc cccccc 697

```

```

<210> 18
<211> 670
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)... (670)
<223> n = A,T,C or G

```

```

<400> 18
ctcgtgtgaa ggggtgcagta cctaagccgg agcggggtag aggcggggccg gcacccccctt 60
ctgacctcca gtgccgcggg cctcaagatc agacatggcc cagaacttga acgacttggc 120
gggacggctg cccgcggggc cccggggcat gggcacggcc ctgaagctgt tgctgggggc 180
cggcgccgtg gcctacgggt tgcgcgaatc tgtgttcacc gtggaaggcg ggcncagagc 240
catcttcttc aatcgggatc gtggagtgc caggacacta tcttggggccg anggccttca 300
cttcaggatc cttggttcca gtaccccanc atctatgaca ttccgggccag acctcgaaaa 360
aatctctccc ctacaggctc caaagacctc cagatggtga atatctccct gcgagtgttg 420
tctcgaccaa tgctcangaa cttcctaaca tgttccancg cctaagggct ggactacnaa 480
gaacgantgt tgccgtccat tgtcacgaag tgctcaagaa tttnggtggc caagttcaat 540
gncctcacnn ctgatcnccc agcggggcca agttanccct ggttgatccc cgggganctg 600
acnnaaaagg gccaaaggact tcccctcatc ctggataatg tggecntcac aaagctcaac 660
tttanccacc 670

```

```

<210> 19
<211> 606
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)... (606)
<223> n = A,T,C or G

```

```

<400> 19
actagtgcc aacctagctc ccaggccagt tctctgaatg tcgaggagtt ccaggatctc 60
tggcctcagt tgtccttggt tattgatggg ggacaaattg gggatggcca gagccccgag 120
tgtcgcttg gctcaactgt ggttgatttg tctgtgcccg gaaagtttg catcattcgt 180
ccaggetgtg cctggaaag tactacagcc atcctccaac agaagtacgg actgctcccc 240
tcacatgogt cctacctgtg aaactctggg aagcaggaag gcccaagacc tgggtgctgga 300
tactatgtgt ctgtccactg acgactgtca aggcctcatt tgcagaggcc accggagcta 360
gggcactagc ctgactttta aggcagtgtg tctttctgag cactgtagac caagcccttg 420
gagctgctgg tttagccttg cacctgggga aaggatgtat ttatttgtat tttcatatat 480
cagccaaaag ctgaatggaa aagttnagaa cattcctagg tggccttatt ctaataagtt 540
tcttctgtct gttttgtttt tcaattgaaa agttattaaa taacagattt agaatctagt 600
gagacc 606

```

```

<210> 20
<211> 449
<212> DNA
<213> Homo sapien

```



```

<400> 20
actagtaaac aacagcagca gaaacatcag tatcagcagc gtcgccagca ggagaatatg      60
cagcgccaga gccgaggaga acccccgctc cctgaggagg acctgtccaa actcttcaaa      120
ccaccacagc cgcctgccag gatggactcg ctgctcattg caggccagat aaacacttac      180
tgccagaaca tcaaggagtt cactgcccac aacttaggca agctcttcac ggcccaggct      240
cttcaagaat acaacaacta agaaaaggaa gtttccagaa aagaagttaa catgaactct      300
tgaagtcaca ccagggaac tcttggaga aatatatttg catattgaaa agcacagagg      360
atctcttttag tgtcattgcc gattttggct ataacagtgt ctttctagcc ataataaaat      420
aaaacaaaat cttgactgct tgctcaaaa      449

```

```

<210> 21
<211> 409
<212> DNA
<213> Homo sapien

```

```

<400> 21
tatcaatcaa ctggtgaata attaaacaat gtgtggtgtg atcatacaaa ggttaccact      60
caatgataaa aggaacaagc tgcctatatg tggaacaaca tggatgcatt tcagaaactt      120
tatgttgagt gaaagaacaa acacggagaa catactatgt ggttctcttt atgtaacatt      180
acagaaataa aaacagaggc aaccaccttt gaggcagtat ggagtgagat agactggaaa      240
aaggaaggaa ggaaactcta cgctgatgga aatgtctgtg tcttcattgg gtggtagtta      300
tgtggggata tacatttgtc aaaattttatt gaactatata ctaaagaact ctgcatttta      360
ttgggatgta aataatacct caattaaaaa gacaaaaaaa aaaaaaaaaa      409

```

```

<210> 22
<211> 649
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (649)
<223> n = A,T,C or G

```

```

<400> 22
acaattttca ttatcttaag cacattgtac atttctacag aacctgtgat tattctcgca      60
tgataaggat ggtacttgca tatggtgaat tactactgtt gacagtttcc gcagaaatcc      120
tatttcagtg gaccaacatt gtggcatggc agcaaatgcc aacattttgt ggaatagcag      180
caaattctaca agagaccctg gttggttttt cgttttgttt tctttgtttt tcccccttc      240
tcctgaatca gcagggatgg aangagggta gggaagtat gaattactcc ttccagtagt      300
agctctgaag tgtcacattt aatatcagtt ttttttaaac atgattctag ttnaatgtag      360
aagagagaag aaagaggaag tgttcacttt tttaatacac tgatttagaa atttgatgtc      420
ttatatcagt agttctgagg tattgatagc ttgctttatt tctgccttta cgttgacagt      480
gttgaagcag ggtgaataac taggggcata tatatttttt ttttttgtaa gctgtttcat      540
gatgttttct ttggaatttc cggataagtt caggaaaaca tctgcatgtt gttatctagt      600
ctgaagttcn tatccatctc attacaacaa aaacncccag aacggnntg      649

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```

<210> 23
<211> 669
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature

```

<222> (1)...(669)

<223> n = A,T,C or G

<400> 23

actagtgccg	tactggctga	aatccctgca	ggaccaggaa	gagaaccagt	tcagactttg	60
tactctcagt	caccagctct	ggaattagat	aaattccttg	aagatgtcag	gaatgggatc	120
tatcctctga	cagcctttgg	gctgcctcgg	ccccagcagc	cacagcagga	ggaggtgaca	180
tcacctgtcg	tgccccctc	tgtcaagact	ccgacacctg	aaccagctga	ggaggagact	240
cgcaaggtgg	tgctgatgca	gtgcaacatt	gagtccggtg	aggaggaggt	caaacaccac	300
ctgacacttc	tgtgaagtt	ggaggacaaa	ctgaaccggc	acctgagctg	tgacctgatg	360
ccaaatgaga	atatccccga	gttggcggct	gagctgggtg	agctgggctt	cattagttag	420
gctgaccaga	gccggttgac	ttctctgcta	gaagagactt	gaacaagttc	aattttgcca	480
ggaacagtac	cctcaactca	gccgctgtca	ccgtctcttc	ttagagctca	ctcgggccag	540
gccctgatct	gcgctgtggc	tgtcctggac	gtgctgcacc	ctctgtcctt	ccccccagtc	600
agtattacct	gtgaagccct	tccctccttt	attattcagg	anggctgggg	gggctccttg	660
nttctaacc						669

<210> 24

<211> 442

<212> DNA

<213> Homo sapien

<400> 24

actagtacca	tcttgacaga	ggatacatgc	tcccaaaacg	tttgttacca	cacttaaaaa	60
tactgcat	cattaagcat	cagtttcaaa	attatagcca	ttcatgattt	actttttcca	120
gatgactatc	attattctag	tcctttgaat	ttgtaagggg	aaaaaaaaca	aaaacaaaaa	180
cttacgatgc	acttttctcc	agcacatcag	atttcaaatt	gaaaattaaa	gacatgctat	240
ggtaatgcac	ttgctagtac	tacacacttt	ggtacaacaa	aaaacagagg	caagaaacaa	300
cggaaagaga	aaagccttcc	tttgttggcc	cttaaaactga	gtcaagatct	gaaatgtaga	360
gatgatctct	gacgatacct	gtatgttctt	attgtgtaaa	taaaattgct	ggtatgaaat	420
gacctaataa	aaaaaaaaga	aa				442

<210> 25

<211> 656

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(656)

<223> n = A,T,C or G

<400> 25

tgcaagtacc	acacactggt	tgaattttgc	acaaaaagtg	actgtaggat	cagggtgatag	60
ccccggaatg	tacagtgtct	tggtgcacca	agatgccttc	taaaggctga	cataccttgg	120
accctaattg	ggcagagagt	atagccctag	cccagtggtg	acatgaccac	tccttttggg	180
aggcctgagg	tagaggggag	tggtatgtgt	tttctcagtg	gaagcagcac	atgagtgggt	240
gacaggatgt	tagataaagg	ctctagttag	ggtgtcattg	tcatttgaga	gactgacaca	300
ctcctagcag	ctggtaaagg	ggtgctggan	gccatggagg	anctctagaa	acattagcat	360
gggctgatct	gattacttcc	tggcatcccg	ctcactttta	tgggaagtct	tattagangg	420
atgggacagt	tttccatata	cttgcctgtg	agctctggaa	cactctctaa	atttccctct	480
attaaaaatc	actgccctaa	ctacacttcc	tccttgaagg	aatagaaatg	gaactttctc	540
tgacatantt	cttggcatgg	ggagccagcc	acaaatgana	atctgaacgt	gtccaggttt	600
ctcctganac	tcattctacat	agaattgggt	aaacctctcc	ttggaataag	gaaaaa	656

<210> 26
 <211> 434
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(434)
 <223> n = A,T,C or G

<400> 26
 actagtctcag actgccacgc caaccccaga aaatacccca catgccagaa aagtgaagtc 60
 ctagggtgtt ccatctatgt ttcaatctgt ccatctacca ggcctcgcga taaaaacaaa 120
 acaaaaaaac gctgccaggt tttagaagca gttctggtct caaaaccatc aggatcctgc 180
 caccagggtt cttttgaaat agtaccacat gtaaaagggga atttggcttt cacttcacat 240
 aataactgaa ttgtcaggct ttgattgata attgtagaaa taagtagcct tctgttgtgg 300
 gaataagtta taatcagtat tcactctctt gttttttgtc actcttttct ctctaattgt 360
 gtcatttgta ctggttgaaa aatatttctt ctatnaaatt aaactaacct gccttaaaaa 420
 aaaaaaaaaa aaaa 434

<210> 27
 <211> 654
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(654)
 <223> n = A,T,C or G

<400> 27
 actagtccaa cacagtcaga aacattgttt tgaatcctct gtaaaccaag gcattaatct 60
 taataaacca ggatccattt aggtaccact tgatataaaa aggatatcca taatgaatat 120
 tttatactgc atcctttaca ttagccacta aatacgttat tgcttgatga agacctttca 180
 cagaatccta tggattgcag catttcactt ggctacttca taccatgcc ttaaagaggg 240
 gcagtttctc aaaagcagaa acatgccgcc agttctcaag ttttcctcct aactccattt 300
 gaatgtaagg gcagctggcc cccaatgtgg ggaggtccga acattttctg aattccatt 360
 ttcttgttcg cggctaaatg acagtttctg tcattactta gattccgatc tttcccaaaag 420
 gtgttgattt acaaagaggc cagctaatag cagaaatcat gacctgaaa gagagatgaa 480
 attcaagctg tgagccaggc agganctcag tatggcaaag gtcttgagaa tcngccattt 540
 ggtacaaaaa aaatttttaa gcntttatgt tataccatgg aaccatagaa anggcaaggg 600
 aattgttaag aanaatttta agtgtccaga ccanaanga aaaaaaaaaa aaaa 654

<210> 28
 <211> 670
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(670)
 <223> n = A,T,C or G

<400> 28
 cgtgtgcaca tactgggagg atttcacag ctgcacggtc acagccctta cggattgcca 60

ggaagggg	cg aaagatatgt	gggataaact	gagaaaagaa	nccaaaaacc	tcaacatcca	120
aggcagctta	ttcgaactct	gcggcagcgg	caacggggcg	gcgggggtccc	tgctcccggc	180
gttcccggtg	ctcctggtgt	ctctctcggc	agcttttagcg	acctgncttt	ccttctgagc	240
gtggggccag	ctcccccg	ggcgccacc	cacnctcact	ccatgctccc	ggaaatcgag	300
aggaagatca	ttagttcttt	ggggacgttn	gtgattctct	gtgatgctga	aaaacactca	360
tatagggaa	gtgggaaatc	ctganctctt	tnttatntcg	tntgatttct	tgtgttttat	420
ttgccaaaat	gttaccaatc	agtgaaccaac	cnagcacagc	caaaaaatcg	acntcngctt	480
tagtccgtct	tcacacacag	aataagaaaa	cggcaaacc	acccacttt	tnantttnat	540
tattactaan	tttttctgt	tgggcaaaag	aatctcagga	acngccctgg	ggccnccgta	600
ctanagttaa	ccnagctagt	tncatgaaaa	atgatgggct	ccnctcaat	gggaaagcca	660
agaaaaagnc						670

<210> 29

<211> 551

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (551)

<223> n = A,T,C or G

<400> 29

actagtcctc	cacagcctgt	gaatccccct	agacctttca	agcatagtga	gcggagaaga	60
agatctcagc	gtttagccac	cttaccatg	cctgatgatt	ctgtagaaaa	ggtttcttct	120
ccctctccag	ccactgatgg	gaaagtattc	tccatcagtt	ctcaaatca	gcaagaatct	180
tcagtaccag	aggtgcctga	tgttgacat	ttgccacttg	agaagctggg	accctgtctc	240
cctcttgact	taagtcgtgg	ttcagaagtt	acagcacgg	tagcctcaga	ttctctttac	300
cgtaatgaat	gtcccagggc	agaaaaagag	gatacncaga	tgcttccaaa	tccttcttcc	360
aaagcaatag	ctgatgggaa	gaggagctcc	agcagcagca	ggaatatcga	aaacagaaaa	420
aaaagtgaat	ttgggaagac	aaaagctcaa	cagcatttgg	taaggagaaa	aganaagatg	480
aggaaggaag	agagaagaga	gacnaagatc	nctacggacc	gnnncggaag	aagaagaagn	540
aaaaaanaaa	a					551

<210> 30

<211> 684

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (684)

<223> n = A,T,C or G

<400> 30

actagttcta	tctggaaaaa	gccggggttg	gaagaagctg	tggagagtgc	gtgtgcaatg	60
cgagactcat	ttcttggaag	catccctggc	aaaaatgcag	ctgagtacaa	ggttatcact	120
gtgatagaac	ctggactgct	ttttgagata	atagagatgc	tgagtctga	agagacttcc	180
agcacctctc	agttgaatga	attaatgatg	gcttctgagt	caactttact	ggctcaggaa	240
ccacgagaga	tgactgcaga	tgtaatcgag	cttaaaggga	aattcctcat	caacttagaa	300
ggtggtgata	ttcgtgaaga	gtcttcctat	aaagtaattg	tcatgccgac	tacgaaagaa	360
aaatgcccc	gttggtggaa	gtatacagcg	ggagtcttca	gatacactgt	gtcctcgatg	420
tgcagaagtt	gtcagtggga	aaatagtatt	aacagctcac	tcgagcaaga	accctcctga	480
cagtactggg	ctagaagttt	ggatggatta	tttacaatat	aggaaagaaa	gccaagaatt	540
aggtnatgag	tggatgagta	aatggtggan	gatggggaat	tcaaatcaga	attatggaag	600

aagttnttcc tggtactata gaaaggaatt atgtttatattt acatgcagaa aatatanatg 660
 tgtggtgtgt accgtggatg gaan 684

<210> 31
 <211> 654
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (654)
 <223> n = A,T,C or G

<400> 31

gcgcagaaaa ggaaccaata tttcagaaac aagcttaata ggaacagctg cctgtacatc	60
aacatcttct cagaatgacc cagaagttat catcgtggga gctggcgtgc ttggctctgc	120
tttggcagct gtgctttcca gagatggaag aaaggtgaca gtcattgaga gagacttaaa	180
agagcctgac agaatagttg gagaattcct gcagccgggt gggtatcatg ttctcaaaga	240
ccttggctctt ggagatacag tgggaaggtct tgatgccag gttgtaaatg gttacatgat	300
tcacatgacag ggaaagcaaa tcagangttc agattcctta ccctctgtca gaaaacaatc	360
aagtgcagag tggaaagact ttccatcacg gaagattcat catgagtctc cggaaagcag	420
ctatggcaga gcccaatgca aagtttattg aaggtgttgt gttacagtta ttagaggaag	480
atgatgttgt gatggagtt cagtacaagg ataaagagac tgggagatat caaggaaactc	540
catgctccac tgactgttgt tgcagatggg cttttctcca anttcaggaa aagcctgggc	600
tcaataaagt ttctgtatca ctcatgtgtg tggcttctta tgaagaatgc nccc	654

<210> 32
 <211> 673
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (673)
 <223> n = A,T,C or G

<400> 32

actagtgaag aaaaagaaat tctgatacgg gacaaaaatg ctcttcaaaa catcattctt	60
tatcacctga caccaggagt ttctattgga aaaggatttg aacctggtgt tactaacatt	120
ttaaagacca cacaaggaag caaaatcttt ctgaaagaag taaatgatac acttctggtg	180
aatgaattga aatcaaaaga atctgacatc atgacaacaa atggtgtaat tcatgttgta	240
gataaactcc tctatccagc agacacacct gttggaaatg atcaactgct ggaaatactt	300
aataaattaa tcaaatacat ccaaattaag tttgttcgtg gtagcacctt caaagaaatc	360
cccgtagctg tctatnagcc aattattaaa aaatacacca aaatcattga tgggagtgcc	420
tgtgggaaat aactgaaaaa gagaccgaga agaacgaatc attacagggtc ctgaaataaa	480
atacctagga tttctactgg aggtggagaa acagaagaac tctgaagaaa ttgttacaaag	540
aagangtccc aaggtcacca aattcattga aggtggtgat ggtctttatt tgaagatgaa	600
gaaattaaaa gacgcttcag ggagacnccc catgaaggaa ttgccagcca caaaaaaatt	660
cagggattag aaa	673

<210> 33
 <211> 673
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (673)
 <223> n = A,T,C or G

<400> 33

actagtttatt	tacttttctc	cgcttcagaa	ggtttttcag	actgagagcc	taagcatact	60
ggatctgttg	tttcttttgg	gtctcacctc	atcagtgtgc	atagtggcag	aaattataaa	120
gaagggttgaa	aggagcaggg	aaaagatcca	gaagcatggt	agttcgacat	catcatcttt	180
tcttgaagta	tgatgcatat	tgcattatct	tatttgcaaa	ctaggaattg	cagtctgagg	240
atcatttaga	agggcaagtt	caagaggata	tgaagatttg	agaacttttt	aactattcat	300
tgactaaaaa	tgaacattaa	tgttnaagac	ttaagacttt	aacctgctgg	cagtcccaaa	360
tgaattatg	caactttgat	atcatattcc	ttgatttaaa	ttgggctttt	gtgattgant	420
gaaactttat	aaagcatatg	gtcagttatt	tnattaaaaa	ggcaaaacct	gaaccacctt	480
ctgcacttaa	agaagtctaa	cagtacaaat	acctatctat	cttagatgga	tntatttntt	540
tntattttta	aatattgtac	tatttatggg	nggtggggct	ttcttactaa	tacacaaatn	600
aatttatcat	ttcaanggca	ttctatttgg	gtttagaagt	tgattccaag	nantgcatat	660
ttcgctactg	tnt					673

<210> 34
 <211> 684
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (684)
 <223> n = A,T,C or G

<400> 34

actagtttat	tcaagaaaag	aacttactga	ttcctctgtt	cctaaagcaa	gagtggcagg	60
tgatcagggc	tggtgtagca	tccggttcct	ttagtgcagc	taactgcatt	tgtcactgat	120
gaccaaggag	gaaatcacta	agacatttga	gaagcagtg	tatgaacgtt	cttggacaag	180
ccacagttct	gagccttaac	cctgtagttt	gcacacaaga	acgagctcca	cctccccctc	240
ttcaggagga	atctgtgcgg	atagattggc	tggacttttc	aatggttctg	ggttgcaagt	300
gggcactgtt	atggctgggt	atggagcgga	cagccccagg	aatcagagcc	tcagcccggc	360
tgcttggtt	gaaggtacag	gtgttcagca	ccttcggaaa	aagggcataa	agtngtgggg	420
gacaattctc	agtccaagaa	gaatgcattg	accattgctg	gctatttgct	tnoctagtat	480
gaattggatn	catttttgac	cangatnntt	ctnctatgct	tnnttgcaat	gaaatcaa	540
ccgcattat	ctacaagtgg	tatgaagtcc	tgcncccccc	agagaggctg	ttcaggcnat	600
gtcttccaag	ggcaggggtg	gttacaccat	ttacctccc	ctctcccccc	agattatgna	660
cncagaagga	atttntttcc	tccc				684

<210> 35
 <211> 614
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (614)
 <223> n = A,T,C or G

<400> 35

actagtccaa	cgcgttngcn	aatattcccc	tggtagccta	cttccttacc	ccogaatatt	60
------------	------------	------------	------------	------------	------------	----

ggtaagatcg	agcaatggct	tcaggacatg	ggttctcttc	tcctgtgac	attcaagtgc	120
tcactgcacg	aagactggct	tgtctcagtg	tntcaacctc	accagggtcg	tctcttggtc	180
cacacctcgc	tcctgttag	tgccgtatga	cagcccccat	canatgacct	tggccaagtc	240
acggtttctc	tgtggtcaat	gttggtnggc	tgattggtgg	aaagtanggt	ggaccaaagg	300
aagncncgtg	agcagncanc	nccagttctg	caccagcagc	gcctccgtcc	tactngggtg	360
ttccngtttc	tcctggccct	gngtgggcta	nggcctgatt	cgggaaanag	cctttgcang	420
gaaggganga	taantgggat	ctaccaattg	attctggcaa	aacnatntct	aagattnttn	480
tgctttatgt	ggganacana	tctantcttc	atttntgtct	gnanatnaca	ccctactcgt	540
gntcgancnc	gtcttcgatt	ttcgganaca	cnccantnaa	tactggcggt	ctgttggtta	600
aaaaaaaaaa	aaaa					614

<210> 36

<211> 686

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (686)

<223> n = A,T,C or G

<400> 36

gtggctggcc	cggttctcgc	cttctcccca	tcccctactt	tcctccctcc	ctccctttcc	60
ctccctcgtc	gactgttgct	tgctggcgcc	agactccctg	accctccctc	caccctcccc	120
taacctcggg	gccaccggat	tgcccttctt	ttcctgttgc	ccagcccagc	cctagtgtca	180
gggcgggggc	ctggagcagc	cggaggcact	gcagcagaag	ananaaaaga	cacgacnaac	240
ctcagctcgc	cagtcgggtc	gctngcttcc	cgccgcatgg	caatnagaca	gacgccgctc	300
acctgctctg	ggcacacgcg	accogtgggt	gatttggcct	tcagtggcat	cacccttatg	360
ggtatttctt	aatcagcgct	tgcaaagatg	gttaacctat	gctacgccag	ggagatacag	420
gagactggat	tggaacattt	ttgggggtcta	aaggtctggt	tgggggtgcaa	cactgaataa	480
ggatgccacc	aaagcagcta	cagcagctgc	agatttcaca	gcccagtggt	gggatgctgt	540
ctcagganag	naattgataa	cctggctcat	aacacattgt	caagaatgtg	gatttcccca	600
ggatattatt	atttggtttac	cggggganag	gataactgtt	tcnctatttt	taattgaaca	660
aactnaaaca	aanctaagg	aatccc				686

<210> 37

<211> 681

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (681)

<223> n = A,T,C or G

<400> 37

gagacanaacn	naacgtcang	agaanaaaaag	angcatggaa	cacaanccag	gcncgatggc	60
caccttccca	ccagcancca	gcgcccccca	gcngccccca	ngnccggang	accangactc	120
cancctgnat	caatctganc	tctattctctg	gccccatncc	acctcggagg	tggangccgn	180
aaaggtcgca	cmnncagaga	agctgctgcc	ancaccancc	gccccnnccc	tgncgggctn	240
nataggaac	tggtgaccnn	gctgcanaat	tcatacagga	gcacgcgang	ggcannnct	300
cacactgagt	tnnngatgan	gcctnaccan	ggacctnccc	cagcnnattg	annacnggac	360
tgccggaggaa	ggaagacccc	gnacnggatc	ctggccggcn	tgccaccccc	ccacccttag	420
gattatnccc	cttgactgag	tctctgaggg	gctacccgaa	ccgcctcca	ttccctacca	480
natnntgctc	natcgggact	gacangctgg	ggatnggagg	ggctatcccc	cancatcccc	540

```

tnanaccaac agcnacngan natnggggct cccnnggggc ggngcaacnc tectncaccc 600
cgggcgnggc ctctgggtgt gtctccntc aacnaattcc naaanggcgg gcccccngt 660
ggactectcn ttgttccctc c 681

```

```

<210> 38
<211> 687
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(687)
<223> n = A,T,C or G

```

```

<400> 38
canaaaaaaa aaaacatggc cgaaaccagn aagctgcgcy atggcgccac ggccctctt 60
ctcccgccct gtgtccggaa ggtttccctc cgaggcgccc cggtcccgcc aagcggagga 120
gagggcgggg cntgcggggg cggagctca naggccctgg ggccgctctg ctctcccgcc 180
atcgcaaggg cggcgctaac ctnaggcctc cccgcaaagg tcccnangc ggnggcggcg 240
gggggctgtg anaaccgcaa aaanaacgct gggcgcgcn gaaacccgct ccccccgcg 300
aaggananac ttccacagan gcagcgtttc cacagccan agccacnttt ctagggtgat 360
gcaccccgat aagtctctgn cggggaagct caccgctgtc aaaaaanctc ttctctccac 420
cggcgcacna aggggangan ggcanganc tgccgcccgc acaggtcatc tgatcacgtc 480
gcccgcctta ntctgctttt gtgaatctcc actttgttca accccacccg ccgttctctc 540
ctcttgcgc ctctctctna ccttaanaac cagcttctc taccnatng tantnctct 600
gcncnngtng aaattaattc ggtccnccgg aacctcttnc ctgtggcaac tgctnaaaga 660
aactgctgtt ctgnttactg cngtccc 687

```

```

<210> 39
<211> 695
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(695)
<223> n = A,T,C or G

```

```

<400> 39
actagtctgg cctacaatag tgtgattcat gtaggacttc tttcatcaat tcaaaacccc 60
tagaaaaacg tatacagatt atataagtag ggataagatt tctaacattt ctgggctctc 120
tgacccctgc gctagactgt ggaaaggag tattattata gtatacaaca ctgctgttgc 180
cttattagtt ataacatgat aggtgctgaa ttgtgattca caatttaaaa aactgtaat 240
ccaaactttt ttttttaact gtagatcatg catgtgaatg ttaatgttaa tttgttcaan 300
gttggtatgg gttagaaaaa ccacatgcct taaaatttta aaaagcaggg cccaaactta 360
ttagtttaaa attaggggta gtgttccagt ttgttattaa ntgggtatag ctctgtttag 420
aanaaatcna ngaacangat ttngaaantt aagntgacat tatttnccag tgacttggtta 480
atltgaaatc anacacggca ccttccgttt tggtnctatt ggnntttgaa tccaancngg 540
ntccaaatct tnttggaac ngtcnntta acttttttac nanatcttat ttttttattt 600
tggaatggcc ctatttaang ttaaaagggg ggggnnccac naccattcnt gaataaaact 660
naatatatat ccttgggtccc ccaaaattta agngg 695

```

```

<210> 40
<211> 674
<212> DNA

```


<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (674)

<223> n = A,T,C or G

<400> 40

actagtagtc agttgggagt ggttgctata ccttgacttc atttatatga atttcactt	60
tattaaataa tagaaaagaa aatcccggtg cttgcagtag agttatagga cattctatgc	120
ttacagaaaa tatagccatg attgaaatca aatagtaaag gctgttctgg ctttttatct	180
tcttagctca tcttaaataa gtagtacact tgggatgcag tgcgtctgaa gtgctaata	240
gttgtaacaa tagcacaaat cgaacttagg atgtgtttct tctcttctgt gtttcgattt	300
tgatcaattc tttaattttg ggaacctata atacagtttt cctattcttg gagataaaaa	360
ttaaatggat cactgatatt taagtcattc tgcttctcat ctnaatattc catattctgt	420
attagganaa antacctccc agcacagccc cctctcaaac cccacccaaa accaagcatt	480
tggaatgagt ctcttttatt tccgaantgt ggatgggtata acccatatcn ctccaatttc	540
tgnttgggtt gggatattaat ttgaactgtg catgaaaagn ggnaatcttt nctttgggtc	600
aaantttncg ggttaatttg nctngncaaa tccaatttnc tttaagggtg tctttataaa	660
atttgcattc cngg	674

<210> 41

<211> 657

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (657)

<223> n = A,T,C or G

<400> 41

gaaacatgca agtaccacac actgtttgaa ttttgacaaa aaagtgactg tagggatcag	60
gtgatagccc cggaatgtac agtgtcttg tgcaccaaga tgccttctaa aggetgacat	120
accttggggc cctaattggg cagagagtat agccctagcc cagtgggtgac atgaccactc	180
cctttgggag gctgaagtta aagggaatgg tatgtgtttt ctcattggaag cagcacatga	240
atnggtnaca ngatgttaaa ntaaggntct antttgggtg tcttgtcatt tgaaaaantg	300
acacactcct ancanctggg aaaggggtgc tggaagccat ggaagaactc taaaaacatt	360
agcatgggct gatctgatta ctctctggca tcccgctcac ttttatggga agtcttatta	420
naaggatggg ananttttcc atatccttgc tgggtggaact ctggaacact ctctaaattt	480
ccctctatta aaaatcactg nccttactac acttctcctt tgganggaata gaaatggacc	540
tttctctgac ttagttcttg gcatggganc cagcccaaat taaaatctga cttntccggt	600
ttctccngaa ctcacctact tgaattggta aaacctcctt tggaattagn aaaaacc	657

<210> 42

<211> 389

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (389)

<223> n = A,T,C or G

<400> 42

```

actagtgtctg aggaatgtaa acaagtttgc tgggccttgc gagacttcac caggttggtt      60
cgatagctca cactcctgca ctgtgcctgt caccaggaa tgtctttttt aattagaaga      120
caggaagaaa acaaaaacca gactgtgtcc cacaatcaga aacctccgtt gtggcagang      180
ggccttcacc gccaccaggg tgtcccgcc gacagggaga gactccagcc ttctgaggcc      240
atcctgaaga attcctgttt gggggttgtg aaggaaaatc acccggtatt aaaaagatgc      300
tggtgcctgc ccgcgtngtn gggaaggagc tggtttctct gtgaatttct taaaagaaaa      360
atattttaag ttaagaaaaa aaaaaaaaaa      389

```

<210> 43

<211> 279

<212> DNA

<213> Homo sapien

<400> 43

```

actagtgaca agtccttggc cttgagatgt cttctcgtta aggagatggg ccttttggag      60
gtaaaggata aatgaatga gttctgtcat gattcactat tctagaactt gcatgacatt      120
tactgtgtta gctctttgaa tgttcttgaa atttttagact ttctttgtta acaataata      180
tgctcttatac attgtataaa agctgttatg tgcaacagtg tggagatcct tgtctgattt      240
aataaaatac ttaaacactg aaaaaaaaaa aaaaaaaaaa      279

```

<210> 44

<211> 449

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(449)

<223> n = A,T,C or G

<400> 44

```

actagtagca tcttttctac aacgttaaaa ttgcagaagt agcttatcat taaaaaacia      60
caacaacaac aataacaata aatcctaagt gttaatcagt tattctaccc cctaccaagg      120
atatcagcct gttttttccc ttttttctcc tgggaataat tgtgggcttc ttcccaaatt      180
tctacagcct ctttcctctt ctcatgcttg agcttccctg tttgcacgca tgcgttgtgc      240
aagantgggc tgtttngctt ggantnccgt ccnagtggaa ncatgcttcc ccttgttact      300
gttgggaagaa actcaaacct tcnancceta ggtgttncca ttttgtcaag tcatcactgt      360
atttttgtac tggcattaac aaaaaaagaa atnaaatatt gttccattaa actttaataa      420
aactttaaaa gggaaaaaaa aaaaaaaaaa      449

```

<210> 45

<211> 559

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(559)

<223> n = A,T,C or G

<400> 45

```

actagtgtgg gggaatcacg gacacttaaa gtcaatctgc gaaataattc ttttattaca      60
cactcactga agtttttgag tcccagagag ccattctatg tcaaacattc caagtactct      120
ttgagagccc agcattacat caacatgccc gtgcagttca aaccgaagtc ogcaggcaaa      180
tttgaagctt tgcttgctat tcaaacagat gaaggcaaga gtattgctat tcgactaatt      240

```

ggtgaagctc	ttggaaaaaa	ttnactagaa	tactttttgt	gttaagttaa	ttacataagt	300
tgtattttgt	taactttatc	tttctacact	acaattatgc	ttttgtatat	atattttgta	360
tgatggatat	ctataattgt	agattttggt	tttacaagct	aatactgaag	actcgactga	420
aatattatgt	atctagccca	tagtattgta	cttaactttt	acagggtgaa	aaaaaaattc	480
tgtgtttgca	ttgattatga	tattctgaat	aaatatggga	atatatttta	atgtgggtaa	540
aaaaaaaaaa	aaaaaggaa					559

<210> 46
 <211> 731
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)... (731)
 <223> n = A,T,C or G

<400> 46						
actagttcta	gtaccatggc	tgctcatagat	gcaaccatta	tattccattt	agtttcttcc	60
tcaggttccc	taacaattgt	ttgaaactga	atatatatgt	ttatgtatgt	gtgtgtgttc	120
actgtcatgt	atatggtgta	tatgggatgt	gtgcagtttt	cagttatata	tatattcata	180
tatacatatg	catatatatg	tataatatac	atatatacat	gcatacactt	gtataatata	240
catatatata	cacatatatg	cacacatatn	atcactgagt	tccaaagtga	gtcttttattt	300
ggggcaattg	tattctctcc	ctctgtctgc	tcactggggc	tttgcaagac	atagcaattg	360
cttgatttcc	tttgataag	agtcttatct	tcggcactct	tgactctagc	cttaacttta	420
gatttctatt	ccagaatacc	tctcatatct	atcttaaaac	ctaaganggg	taaagangtc	480
ataagattgt	agtatgaaag	antttgctta	gttaaattat	atctcaggaa	actcattcat	540
ctacaaatta	aattgtaaaa	tgatggtttg	ttgtatctga	aaaaatgttt	agaacaagaa	600
atgtaactgg	gtacctgtta	tatcaaagaa	cctcnattta	ttaagtctcc	tcatagccan	660
atccttatat	ngccctctct	gacctgantt	aatananact	tgaataatga	atagttaatt	720
taggnttggg	c					731

<210> 47
 <211> 640
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)... (640)
 <223> n = A,T,C or G

<400> 47						
tgcgngccgg	tttggccctt	ctttgtanga	cactttcate	cgccctgaaa	tcttcccgat	60
cgtttaataac	tcctcaggtc	cctgcctgca	caggggtttt	tcttantttg	ttgcctaaca	120
gtacacaaa	tgtgacatcc	tttccaat	atngattnct	tcataaccaca	tentcnatgg	180
anacgactnc	aacaattttt	tgatnaccen	aaanactggg	ggetnnaana	agtacantct	240
ggagcagcat	ggacctgtcn	gcnactaang	gaacaanagt	nntgaacatt	tacacaacct	300
ttggtatgtc	ttactgaaag	anagaaacat	gcttctnncc	ctagaccacg	aggncaaccg	360
caganattgc	caatgccaaag	tccgagcggg	tagatcagggt	aatacattcc	atggatgcac	420
tacatacnnt	gtccccgaaa	nanaagatgc	cctaanggct	tcttcanact	ggtccngaaa	480
acancatcac	ctggtgcttg	ganaacanac	tctttggaag	atcatctggc	acaagttccc	540
cccagtgggg	tttnccttgg	cacctanctt	accanactna	ttcggaance	attctttggc	600
ntggcnttnt	nttgggacca	ntcttctcac	aactgnaccc			640

<210> 48
 <211> 257
 <212> DNA
 <213> Homo sapien

<400> 48

actagtatat gaaaatgtaa atatcacttg tgtactcaaa caaaagttgg tcttaagctt	60
ccaccttgag cagccttgga aacctaacct gcctctttta gcataatcac attttctaaa	120
tgattttctt tgttcctgaa aaagtgattt gtattagttt tacatttggt ttttggaaga	180
ttatatttgt atatgtatca tcataaaaata tttaaataaa aagtatcttt agagtgaata	240
aaaaaaaaa aaaaaaa	257

<210> 49
 <211> 652
 <212> DNA
 <213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (652)

<223> n = A,T,C or G

<400> 49

actagttcag atgagtggct gctgaagggg ccccttgc attttcatta taaccaatt	60
tcacttatt tgaactctta agtcataaat gtataatgac ttatgaatta gcacagttaa	120
gttgacacta gaaactgccc atttctgtat tacactatca aataggaaac attggaaga	180
tggggaaaaa aatcttattt taaaatggct tagaaagttt tcagattact ttgaaaatc	240
taaacttctt tctgtttcca aaacttgaaa atatgtagat ggactcatgc attaagactg	300
ttttcaaagc tttcctcaca tttttaaagt gtgattttcc ttttaataa catatttatt	360
ttctttaag cagctatata ccaacccatg actttggaga tatacctatn aaaccaatat	420
aacagcangg ttattgaagc agctttctca aatgttgctt cagatgtgca agttgcaaat	480
tttattgtat ttgtanaata caattttgt tttaaactgt atttcaatct atttctcaa	540
gatgcttttc atatagagtg aaatatccca ngataactgc ttctgtgtcg tcgcatttga	600
cgcataactg cacaatgaa cagtgtatac ctcttggttg tgcattnacc cc	652

<210> 50
 <211> 650
 <212> DNA
 <213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (650)

<223> n = A,T,C or G

<400> 50

ttgcgctttg attttttttag ggcttgtgcc ctgtttcact tatagggtct agaagcttg	60
tgttgagtaa aaaggagatg cccaatatc aaagctgcta aatgttctct ttgccataaa	120
gactccgtgt aactgtgtga acacttggga tttttctcct ctgtcccgag gtctgcgtct	180
gctttctttt ttgggttctt tctagaagat tgagaaatgc atatgacagg ctgagancac	240
ctccccaaac acacaagctc tcagccacan gcagcttctc cacagcccca gcttcgcaca	300
ggctcctgga nggctgcctg ggggaggcag acatgggagt gccaagggtg ccagatggtt	360
ccaggactac aatgtcttta ttttaactg tttgccactg ctgccctcac ccctgcccgg	420
ctctggagta ccgtctgccc canacaagtg ggantgaaat ggggggtggg gggaaactg	480
attcccantt aggggggtgcc taactgaaca gtagggtatan aaggtgtgaa cctgngaant	540

gcttttataa attatnttcc ttgttanatt tatttttttaa tttaattctct gttnaactgc 600
ccngggaaaa ggggaaaaaa aaaaaaaat tctntttaaa cacatgaaca 650

<210> 51
<211> 545
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(545)
<223> n = A,T,C or G

<400> 51
tggcgtgcaa ccagggtagc tgaagtttgg gtctgggact ggagattggc cattaggcct 60
cctganattc cagctccctt ccaccaagcc cagtcttgct acgtggcaca gggcaaacct 120
gactcccttt gggeectcagt tccccctccc cttcatgana tgaaaagaat actacttttt 180
cttggtggtc taacnttget ggacncaaag tgtngtcatt attgttgat tgggtgatgt 240
gtncaaaact gcagaagctc actgcctatg agaggaanta agagagatag tggatganag 300
ggacanaagg agtcattatt tggatatagat ccaccntcc caacctttct ctcctcagtc 360
cctgcncctc atgtntctgg tntggtgagt cctttgtgcc accanccatc atgctttgca 420
ttgctgccat cctgggaagg ggggtgnatcg tctcacaact tgttgtcatc gtttganatg 480
catgctttct tnatnaaaca aanaaannaa tgtttgacag ngtttaaaat aaaaaanaaa 540
caaaa 545

<210> 52
<211> 678
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(678)
<223> n = A,T,C or G

<400> 52
actagtagaa gaactttgce gcttttgtgc ctctcacagg cgcctaaagt cattgccatg 60
ggaggaagac gatttggggg gggagggggg gggggcangg tccgtggggc ttccctant 120
ntatctccat ntccantggn cnntgtgcgc tcttccctcg tcn cattnga anttantccc 180
tggnecccn nccctctecn nccnncnct cccccctcg ncnccctcnn cttttntan 240
ncttcccat ctcnctccc cctnanngtc ccaacnccgn cagcaatnnc ncaattnctc 300
nctcncncc tcnnccggtt cttctnttct cnacntntnc ncnntnecn tgcnnntnaa 360
annctctccc cnetgcaanc gattctctcc ctcnncnnan ctntccactc cntncttctc 420
nncgctcct nttctcnnc ccacctctcn ccttcgnccc cantacnctc ncncccttn 480
cgnntenttn nnntcctcnn accnccncc tcccttcncc cctcttctcc cgggtntntc 540
tetctccnnc nncnncnct cnnccntcc nngcgnccnt ttccgccccn cncnccntt 600
ccttctcnc cantccatcn cntntnccat nctnccncc nctcacnccc gctnccccn 660
ntctctttca caengtec 678

<210> 53
<211> 502
<212> DNA
<213> Homo sapien

<220>

<221> misc_feature
 <222> (1) ... (502)
 <223> n = A,T,C or G

<400> 53
 tgaagatcct ggtgtcgcca tgggcccgcg ccccgcccgt tgttaccggt attgtaagaa 60
 caagccgtac ccaaagtctc gcttctgccg aggtgtccct gatgccaaaa ttgcattttt 120
 tgacctgggg cggaaaaang caaaantgga tgagtctccg ctttgtggcc acatgggtgc 180
 agatcaatat gagcagctgt cctctgaagc cctgnangct gcccgaaattt gtgccaataa 240
 gtacatggta aaaagtngtg gcnaagatgc ttccatatcc ggggtcggnt ccaccccttc 300
 cacgtcatcc gcatcaacaa gatgttgctc tgtgctgggg ctgacaggct cccaacaggc 360
 atgccaagtg cctttggaaa acccanggca ctgtggccag gggtcacatt gggccaattn 420
 atcatgttca tccgcaccaa ctgcagaaca angaacntgt naattnaagc cctgcccagg 480
 gncaanttca aatttcccgg cc 502

<210> 54
 <211> 494
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (494)
 <223> n = A,T,C or G

<400> 54
 actagtccaa gaaaaatatg cttaatgtat attacaaagg ctttgtatat gttaacctgt 60
 tttaatgccaa aaagtgtgct ttgtccacaa ttctcttaag acctcttcag aaagggattt 120
 gtttgccctta atgaatactg ttgggaaaaa acacagtata atgagtgaag agggcagaag 180
 caagaaattt ctacatctta gcgactccaa gaagaatgag tatccacatt tagatggcac 240
 attatgagga ctttaatctt tccttaaaca caataatgtt ttcttttttc ttttattcac 300
 atgatttcta agtatatttt tcatgcagga cagtttttca acctgatgt acagtgactg 360
 tgttaaattt ttctttcagt ggcaacctct ataacttta aaatatgggt agcatcttgt 420
 ctgttttgaa ngggatatga cnatnaatct atcagatggg aaatcctgtt tccaagttag 480
 aaaaaaaaaa aaaa 494

<210> 55
 <211> 606
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (606)
 <223> n = A,T,C or G

<400> 55
 actagtaaaa agcagcattg ccaaataatc cctaattttc cactaaaaat ataatgaat 60
 gatgttaagc tttttgaaaa gttaggtta aacctactgt tgtagatta atgtatttgt 120
 tgcttccctt tatctggaat gtggcattag cttttttatt ttaaccctct ttaattctta 180
 ttcaattcca tgacttaagg ttggagagct aaacactggg atttttggat aacagactga 240
 cagttttgca taattataat cggcattgta catagaaagg atatggctac cttttgttaa 300
 atctgcactt tctaaatata aaaaaaggga aatgaagtat aaatcaattt ttgtataatc 360
 tgtttgaaac atgantttta tttgcttaat attanggtt tgcccttttc tgttagtctc 420
 ttgggatcct gtgtaaaact gttctcatta aacaccaaac agttaagtcc attctctggt 480

```

actagctaca aattccgttt catattctac ntaacaatth aaattaactg aaatatttct 540
anatgggtcta cttctgtcnt ataaaaacna aacttgantt nccaaaaaaa aaaaaaaaaa 600
aaaaaa 606

```

<210> 56

<211> 183

<212> DNA

<213> Homo sapien

<400> 56

```

actagtatat ttaaaacttac aggcttattt gtaatgtaaa ccaccatttt aatgtactgt 60
aattaacatg gttataatac gtacaatcct tccctcatcc catcacacaa ctttttttgt 120
gtgtgataaa ctgatttttg tttgcaataa aaccttgaaa aataaaaaaa aaaaaaaaaa 180
aaa 183

```

<210> 57

<211> 622

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (622)

<223> n = A,T,C or G

<400> 57

```

actagtcact actgtcttct ccttgtagct aatcaatcaa tattcttccc ttgcctgtgg 60
gcagtggaga gtgctgctgg gtgtacgctg cacctgccca ctgagttggg gaaagaggat 120
aatcagtgag cactgttctg ctgagagctc ctgatctacc ccaccccta ggatccagga 180
ctgggtcaaa gctgcatgaa accaggccct ggcagcaacc tgggaatggc tggaggtggg 240
agagaacctg acttctcttt cctctccct cctccaacat tactggaact ctatcctgtt 300
agggatcttc tgagcttggt tccctgctgg gtgggacaga agacaaagga gaagggangg 360
tctacaanaa gcagcccttc tttgtcctct ggggttaatg agcttgacct ananttcag 420
gaganaccan aagcctctga ttttaattt ccntnaaatg tttgaagtnt atatntacat 480
atatatattt ctttnaatnt ttgagtcctt gatatgtctt aaaatccant ccctctgcn 540
gaaacctgaa ttaaaacct gaanaaaaat gtttncctta aagatgttan taattaattg 600
aaacttgaaa aaaaaaaaaa aa 622

```

<210> 58

<211> 433

<212> DNA

<213> Homo sapien

<400> 58

```

gaacaaattc tgattggtta tgtaccgtca aaagacttga agaaatttca tgattttgca 60
gtgtggaagc gttgaaaatt gaaagtact gcttttccac ttgctcatat agtaaaggga 120
tcctttcagc tgccagtgtt gaataatgta tcatccagag tgatgttatc tgtgacagtc 180
accagcttta agctgaacca ttttatgaat accaaataaa tagacctctt gtactgaaaa 240
catatttggt actttaatcg tgctgcttg atagaaatat ttttactggg tcttctgaat 300
tgacagtaaa cctgtccatt atgaatggcc tactgttcta ttatttggtt tgacttgaat 360
ttatccacca aagacttcat ttgtgtatca tcaataaagt tgtatgttcc aactgaaaaa 420
aaaaaaaaa aaa 433

```

<210> 59

<211> 649

<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(649)
<223> n = A,T,C or G

<400> 59

actagttatt atctgacttt cngggtataa tcattcta	gagtggtgaag tagcctctgg	60
tgtcatttgg atttgcat	ctctgatgag tgatgctatc aagcaccttt gctgggtgctg	120
ttggccatat gtgtatgttc cctggagaag	tgtctgtgct gagccttggc ccacttttta	180
attaggcgtn tgtcttttta ttactgagtt	gtaaganttc tttatatatt ctggattcta	240
gacccttate agatacatgg ttgcaaata	ttttctccca ttctgtgggt tgtgttttca	300
ctttatcgat aatgtcctta gacatataat	aaatttgtat tttaaaagtg acttgatttg	360
ggctgtgcaa ggtgggctca ogcttgta	at cccagcactt tgggagactg aggtgggtgg	420
atcatatgan gangctagga gtteggaggtc	agcctggcca gcatagcgaa aacttgtctc	480
tacnaaaaat acaaaaatta gtcaggcatg	gtgggtgcacg tctgtaatac cagcttctca	540
ggangctgan gcacaaggat cacttgaacc	ccagaangaa gangttgcag tganctgaag	600
atcatgccag ggcaacaaaa atgagaactt	gtttaaaaaa aaaaaaaaaa	649

<210> 60
<211> 423
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(423)
<223> n = A,T,C or G

<400> 60

actagttcag gccttcag	tcactgacaa acatggggaa gtgtgccag	ctggctggaa	60
acctggcag	gataccatca agcctgatgt ccaaaagagc	aaagaatatt tctccaagca	120
gaagtgagcg	ctgggctggt ttagtgccag	gctgcggtgg gcagccatga	gaacaaaacc 180
tcttctgtat	tttttttttc cattagtana	acacaagact cngattcagc	cgaattgtgg 240
tgtcttacaa	ggcagggctt	tcctacaggg ggtgganaaa	acagcctttc
aggaatggcc	tgagttggcg	ttgtgggcag gctactggtt	tgtatgatgt
caaccatta	atcttttgta	gtttgtatna aacttganct	gagaccttaa
aaa		acaaaaaaaaa	423

<210> 61
<211> 423
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(423)
<223> n = A,T,C or G

<400> 61

cgggactgga atgtaaagtg	aagttcggag ctctgagcac	gggctcttcc	cgccgggtcc	60
tcctcccga	gacccagag	ggagaggccc	accccgcca	gccccgccc
caggtctgag	tatggctggg	agtcgggggc	cacaggcctc	tagctgtgct
			gctcaagaag	180


```

actggatcag ggtanctaca agtggccggg ccttgccctt gggattctac cctgttccta 240
atttggtgtt ggggtgcggg gtccctggcc cccttttcca cactnccctc ctccngacag 300
caacctccct tggggcaatt gggcctggnt ctcnccccgn tgttgcnaac ctttgttggt 360
ttaaggncct taaaaatgtt annttttccc ntgcncgggt taaaaaagga aaaaactnaa 420
aaa 423

```

```

<210> 62
<211> 683
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(683)
<223> n = A,T,C or G

```

```

<400> 62
gctggagagg ggtacggact ttcttggagt tgtcccaggt tggaaatgaga ctgaactcaa 60
gaagagaccc taagagactg gggaaatggtt cctgccttca ggaaagtga agacgcttag 120
gctgtcaaca cttaaaggaa gtccccctga agcccagagt ggacagacta gacccattga 180
tggggccact ggccatggc cgtggacaag acattccngt gggccatggc acaccggggg 240
ggatcaaaat gtgtacttgt ggggtctcgc cccttgccaa aaccaaacca ntccactcc 300
tgtcnttggga ctttcttccc attccctcct ccccaaatgc acttcccctc ctccctctgc 360
ccctcctgtg tttttggaat tctgtttccc tcaaaattgt taatttttta nttttngacc 420
atgaacttat gtttggggtc nangttcccc ttccaatgc atactaatat attaatggtt 480
atttattttt gaaatatttt ttaatgaact tggaaaaaat tnntggaatt tccttncttc 540
cntttntttt ggggggggtg gggggntggg ttaaaatttt tttggaancc cnatnggaaa 600
ttnttacttg gggccccctc naaaaaantn anttccaatt cttnnatngc cctnttccn 660
ctaaaaaaa ananannaaa aan 683

```

```

<210> 63
<211> 731
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(731)
<223> n = A,T,C or G

```

```

<400> 63
actagtcata aagggtgtgc gcgtcttcga cgtggcggtc ttggcgccac tgctgcgaga 60
cccggccctg gacctcaagg tcatccactt ggtgcgtgat cccgcgcggg tggcgagttc 120
acggatccgc tcgcgccacg gcctcatccg tgagagccta cagggtgtgc gcagccgaga 180
ccgcgagctc accgcatgcc cttcttggag gccgcgggcc acaagcttgg cggccanaaa 240
gaaggcgtng ggggcccga aantaccacg ctctggcggc tatggaangt cctcttgcaa 300
taatattggt tnaaaantcg canaanagcc cctgcanccc cctgaactgg gntgcagggc 360
cncttacctn gtttgntgc ggttacaaag aacctgttn ggaaaaccct nccnaaaacc 420
ttccgggaaa attntncaaa ttttnttgg ggaattnttg ggtaaacccc ccnaaaatgg 480
gaaacntttt tgcctnmaa antaaacat tnggttccgg gggccccccc ncaaaaccct 540
ttttntttt tttntgcccc cantnncccc ccggggcccc ttttttngg ggaaaanccc 600
ccccctncc nanantttta aaagggnggg anaatttttn ntncccccc gggncccccn 660
ggngntaaaa nggtttcncc ccccgaggg gnggggnnnc ctcnnaaacc cntntcnna 720
ccncttttn n 731

```

<210> 64
 <211> 313
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(313)
 <223> n = A,T,C or G

<400> 64
 actagttgtg caaaccacga ctgaagaaag acgaaaagtg ggaaataact tgcaacgtct 60
 gttagagatg gttgctacac atgttgggtc tgtagagaaa catcttgagg agcagattgc 120
 taaagttgat agagaatatg aagaatgcat gtcagaagat ctctcggaaa atattaaaga 180
 gattagagat aagtatgaga agaaagctac tctaattaag tcttctgaag aatgaagatn 240
 aaatgttgat catgtatata tatccatagt gaataaaatt gtctcagtaa agttgtaaaa 300
 aaaaaaaaaa aaa 313

<210> 65
 <211> 420
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(420)
 <223> n = A,T,C or G

<400> 65
 actagttccc tggcaggcaa gggcttccaa ctgaggcagt gcatgtgtgg cagagagagg 60
 caggaagctg gcagtggcag cttctgtgtc tagggagggg tgtggctccc tecttccctg 120
 tctgggaggt tggagggaaag aatctaggcc ttagcttgcc ctctgccac ctttccctt 180
 gtagatactg ccttaacact cctcctcttc tcagctgtgg ctgccacca agccaggttt 240
 ctccgtgctc actaatttat ttccaggaaa ggtgtgtgga agacatgagc cgtgtataat 300
 atttgtttta acattttcat tgcaagtatt gaccatcatc cttgggtgtg tatcgttgta 360
 acacaaatta atgatattaa aaagcatcca aacaaagccn annnnnaana nnannngaaa 420

<210> 66
 <211> 676
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(676)
 <223> n = A,T,C or G

<400> 66
 actagtttcc tatgatcatt aaactcattc tcagggttaa gaaaggaatg taaatttctg 60
 cctcaatttg tacttcatca ataagttttt gaagagtgcg gatttttagt caggtcttaa 120
 aaataaaactc acaaatctgg atgcatttct aaattctgca aatgtttcct ggggtgactt 180
 aacaaggaat aatcccacaa tatacctagc tacctaatac atggagctgg ggtcaaccc 240
 actgttttta aggatttgcg cttacttgtg gctgaggaaa aataagtagt tccgagggaa 300
 gtagttttta aatgtgagct tatagatngg aaacagaata tcaacttaat tatggaaatt 360
 gtagaaaacc tgttctcttg ttatctgaat cttgattgca attactattg tactggatag 420

actccagccc attgcaaagt ctcagatata ttanctgtgt agttgaattc cttggaaatt	480
ctttttaaga aaaaattgga gtttnaaaga aataaacccc tttgttaaata gaagcttggc	540
tttttgggtga aaaanaatca tccgcaggg cttattgttt aaaaanggaa ttttaagcct	600
ccctggaaaa anttgtaata taaatgggga aaatgntggg naaaaattat ccgttagggt	660
ttaaagggaa aactta	676

<210> 67

<211> 620

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(620)

<223> n = A,T,C or G

<400> 67

caccattaaa gctgcttacc aagaacttcc ccagcatttt gacttccttg tttgatagct	60
gaattgtgag caggtgatag aagagccttt ctagttgaac atacagataa tttgctgaat	120
acattccatt taatgaaggg gttacatctg ttacgaagct actaagaagg agcaagagca	180
taggggaaaa aaatctgata agaacgcata aaactcacat gtgccccctc tactacaaac	240
agattgtagt gctgtgggtg tttattccgt tgtgcagaac ttgcaagctg agtcactaaa	300
cccaaagaga ggaaattata ggtagttaa acattgtaat ccaggaact aagtttaatt	360
cacttttgaa gtgttttgtt tttattttt ggttgtctg atttactttg ggggaaaang	420
ctaaaaaaa agggatatca atctctaatt cagtgcccac taaaagttgt ccctaaaaag	480
tctttactgg aanttattgg actttttaag ctccaggtnt tttggtcctc caaattaacc	540
ttgcatgggc cccttaaaat tgttgaangg cattcctgcc tctaagtttg gggaaaattc	600
ccccnttttn aaaatttga	620

<210> 68

<211> 551

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(551)

<223> n = A,T,C or G

<400> 68

actagtagct ggtacataat cactgaggag ctatttctta acatgctttt atagaccatg	60
ctaagtctag accagtattt aagggtctaat ctacacctc cttagctgta agagtctggc	120
ttagaacaga cctctctgtg caataacttg tggccactgg aaatccctgg gccggcattt	180
gtattgggggt tgcaatgact cccaagggcc aaaagagtta aaggcacgac tgggatttct	240
tctgagactg tgggtgaaact ccttccaagg ctgaggggggt cagtangtgc tctgggaggg	300
actcggcacc actttgatat tcaacaagcc acttgaagcc caattataaa attgttattt	360
tacagctgat ggaactcaat ttgaaccttc aaaactttgt tagtttatcc tattatattg	420
ttaaacctaa ttacatttgt ctagcattgg atttgggtcc tgtngcatat gttttttcn	480
cctatgtgct cccctcccc nnatcttaat ttaaaccnca attttgcnat tcnccnnnnn	540
nannnnanna a	551

<210> 69

<211> 396

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(396)

<223> n = A,T,C or G

<400> 69

cagaaatgga aagcagagtt ttcattttctg tttataaaacg tctccaaaca aaaatggaaa	60
gcagagtttt cattaaatcc ttttaccttt tttttttctt ggtaatcccc tcaaataaca	120
gtatgtggga tattgaatgt taaagggata tttttttcta ttatttttat aattgtacaa	180
aattaagcaa atgttaaaag ttttatatgc tttattaatg ttttcaaaag gtatnatata	240
tgtgatacat tttttaagct tcagttgctt gtcttctggt actttctggt atgggctttt	300
ggggagccan aaaccaatct acnatctctt tttgtttgcc aggacatgca ataaaattta	360
aaaaataaat aaaaactatt nagaaattga aaaaaa	396

<210> 70

<211> 536

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(536)

<223> n = A,T,C or G

<400> 70

actagtgcaa aagcaaatat aaacatcgaa aaggcggtcc tcacgttagc tgaagatata	60
cttcgaaaga cccctgtaaa agagcccaac agtgaaaatg tagatatcag cagtggagga	120
ggcgtgacag gctggaagag caaatgctgc tgagcattct cctgttccat cagttgccat	180
ccactacccc gttttctctt cttgctgcaa aataaaccac tctgtccatt ttaactcta	240
aacagatatt tttgtttctc atcttaacta tccaagccac ctattttatt tgttctttca	300
tctgtgactg cttgctgact ttatcataat tttcttcaaa caaaaaaatg tatagaaaaa	360
tcatgtctgt gacttcattt ttaaatgnta cttgctcagc tcaactgcat ttcagttggt	420
ttatagtcca gttcttatca acattnaaac ctatngcaat catttcaaat ctattctgca	480
aattgtataa gaataaaagt tagaatttaa caattaaaaa aaaaaaaaaa aaaaaa	536

<210> 71

<211> 865

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(865)

<223> n = A,T,C or G

<400> 71

gacaaagcgt taggagaaga anagaggcag ggaanactnc ccaggcacga tggccnctt	60
cccaccagca accagcgccc cccaccagcc cccaggcccg gacgacgaag actccatcct	120
ggattaatct nacctctntc gcctgnccca ttcctacctc ggaggtggag gccggaaagg	180
tcncaccaag aganaanctg ctgccaacac caaccgcccc agccctggcg ggcagganag	240
gaaactggtg accaatctgc agaattctna gaggaanaag cnaggggccc cgcgctnaga	300
cagagctgga tatgangcca gaccatggac nctacnccn ncaatncana cgggactgcy	360
gaagatggan gaccncgac nngatcagge cngctnncca nccccccacc cctatgaatt	420
attccogctg aangaatctc tgannggctt ccannaaagc gcctccccnc cnaacgnaan	480

tncaacatng	ggattanang	ctgggaactg	naaggggcaa	ancctnnaat	atccccagaa	540
acaanctctc	ccnaanaaac	tggggcncct	catnggtggn	accaactatt	aactaaaccg	600
cacgccaagn	aantataaaa	ggggggcccc	tccnccgngn	accccccttt	gtcccttaat	660
ganggttatc	cnccttgctg	accatgggtc	ccmmttctgt	ntgnatgttt	ccnctccccct	720
ccnctatnt	cnagccgaac	tcnnatttnc	ccgggggtgc	natcnantng	tncncccttn	780
ttngttgncc	cngccctttc	cgnccggaacn	cgtttccccc	ttantaacgg	cacccgggggn	840
aagggtgntt	ggccccctcc	ctccc				865

<210> 72

<211> 560

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(560)

<223> n = A,T,C or G

<400> 72

cctggacttg	tcttggttcc	agaacctgac	gacccggcga	cggcgacgtc	tcttttgact	60
aaaagacagt	gtccagtgtc	ccngcctagg	agtctacggg	gaccgcctcc	cgcgcgccca	120
ccatgcccaa	cttctctggc	aactggaaaa	tcacccgac	ggaaaacttc	gangaattgc	180
tcnaantgct	gggggtgaat	gtgatgctna	ngaanattgc	tgtggctgca	gcgtccaagc	240
cagcagtggg	gatcnaacag	gaggagagaca	ctttctacat	caaaacctcc	accacogtgc	300
gcaccacaaa	gattaacttc	nnngttgggg	aggantttga	ggancaaact	gtggatngga	360
ngcctgtnaa	aacctggtga	aatgggagaa	tganaataaa	atggtctgtg	ancanaaact	420
cctgaaagga	gaaggccccc	anaactcctg	gaccngaaaa	actgaccnc	cnatngggga	480
actgatnctt	gaaccctgaa	cgggcgggat	ganccctttt	tnttgcncnc	naanggggtc	540
tttcnntttc	cccaaaaaaa					560

<210> 73

<211> 379

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(379)

<223> n = A,T,C or G

<400> 73

ctggggancc	ggcggtnngc	nccatntcnn	gncgcgaagg	tggcaataaa	aanccnctga	60
aaccgcncaa	naaacatgcc	naagatatgg	acgaggaaga	tnngctttc	nngnacaanc	120
gnanngagga	acanaacaaa	ctcnangagc	tctcaagcta	atgccgcggg	gaagggggccc	180
ttggccacnn	gtggaattaa	gaaatctggc	aaanngtann	tgttccttgt	gcctnangag	240
ataagngacc	ctttatttca	tctgtattta	aacctctctn	ttccctgnca	taacttcttt	300
tnccacgtan	agntggaant	anttggtgtc	ttggactgtt	gtncatttta	gannaaactt	360
ttgttcaaaa	aaaaaataa					379

<210> 74

<211> 437

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature
 <222> (1)...(437)
 <223> n = A,T,C or G

<400> 74

actagttcag	actgccacgc	caaccccaga	aaatacccca	catgccagaa	aagtgaagtc	60
ctaggtgttt	ccatctatgt	ttcaatctgt	ccatctacca	ggcctcgca	taaaaacaaa	120
acaaaaaac	gctgccagg	tttanaagca	gttctggct	caaaaccatc	aggatcctgc	180
caccaggggt	cttttgaaat	agtaccacat	gtaaaagga	atttggcttt	cacttcatt	240
aatcactgaa	ttgtcaggct	ttgattgata	attgtagaaa	taagtagcct	tctgttggtg	300
gaataagtta	taatcagtat	tcattctctt	gttttttgc	actcttttct	ctctnattgt	360
gtcatttgta	ctggttgaaa	aatatttctt	ctataaaatt	aaactaacct	gccttaaaaa	420
aaaaaaaaa	aaaaaaaaa					437

<210> 75
 <211> 579
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(579)
 <223> n = A,T,C or G

<400> 75

ctccgtcgcc	gccaaagatga	tgtgcggggc	gccctccgcc	acgcagccgg	ccaccgcga	60
gaccagcac	atcgccgacc	aggtgaggtc	ccagcttgaa	gagaaagaaa	acaagaagtt	120
ccctgtgttt	aaggccgtgt	cattcaagag	ccaggtggtc	gcggggacaa	actacttcat	180
caaggtgcac	gtcggcgacg	aggacttcgt	acacctgcga	gtgttccaat	ctctccctca	240
tgaaaacaag	cccttgacct	tatctaacta	ccagaccaac	aaagccaagc	atgatgagct	300
gacctatttc	tgatcctgac	tttgacaag	gcccttcagc	cagaagactg	acaaagtcatt	360
cctccgtcta	ccagagcgtg	cacttgatg	cctaaaataa	gcttcattct	cgggctgtgc	420
ccttgggggtg	gaaggggcan	gatctgcact	gcttttgcatt	ttctcttcct	aaatttcatt	480
gtgttgattc	tttcttcca	ataggtgatc	tttattactt	tcagaatatt	ttccaaatna	540
gatataattt	naaaatcctt	aaaaaaaaa	aaaaaaaaa			579

<210> 76
 <211> 666
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(666)
 <223> n = A,T,C or G

<400> 76

gtttatctta	tctctccaac	cagattgtca	gctccttgag	ggcaagagcc	acagtatatt	60
tcctgtttc	ttccacagt	cctaataata	ctgtggaact	aggttttaatt	aattttttaa	120
ttgatgttgt	tatgggcagg	atggcaacca	gaccattgtc	tcagagcagg	tgtctggctct	180
ttcctggcta	ctccatgttg	gctagcctct	ggtaacctct	tacttattat	cttcaggaca	240
ctcactacag	ggaccaggga	tgatgcaaca	tccttgtctt	tttatgacag	gatgtttgct	300
cagcttctcc	aacaataaaa	agcacgtgg	aaaacacttg	cggatattct	ggactgtttt	360
taaaaaatat	acagtttacc	gaaaatcata	ttatcttaca	atgaaaagga	ntttatagat	420
cagccagtga	acaacctttt	cccaccatac	aaaaattcct	tttcccgaa	gaaaanggct	480

ttctcaataa nectcacttt cttaanatct tacaagatag ccccganatc ttatcgaaac	540
tcatttttagg caaatatgan ttttattgtt cgttacttgt ttcaaaattt ggtattgtga	600
atatcaatta ccaccccat ctcccatgaa anaaanggga aanggtgaan ttcntaancg	660
cttaaa	666

<210> 77

<211> 396

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (396)

<223> n = A,T,C or G

<400> 77

ctgcagcccg ggggatccac taatctacca nggttatttg gcagctaatt ctanatttgg	60
atcattgccc aaagttgcac ttgctgggtct cttgggattt ggccttggaa aggtatcata	120
catanganta tgccanaata aattccattt ttttgaaaat canctccttg ggcctgggtt	180
tggtccacag cataacangc actgcctcct tacctgtgag gaatgcaaaa taaagcatgg	240
attaagttag aaggagact ctgagccttc agcttcctaa attctgtgtc tgtgactttc	300
gaagtttttt aaacctctga atttgtacac attttaaatt tcaagtgtac tttaaaataa	360
aatacttcta atgggaacaa aaaaaaaaaa aaaaaa	396

<210> 78

<211> 793

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (793)

<223> n = A,T,C or G

<400> 78

gcattcctagc cgccgactca cacaaggcag gtgggtgagg aaatccagag ttgccatgga	60
gaaaattcca gtgtcagcat tcttgtcctc tgtggccctc tcctacactc tggccagaga	120
taccacagtc aaacctggag ccaaaaagga cacaaggac tctcgacceca aactgccccca	180
gacctctctc agaggttggg gtgaccaact catctggact cagacatagt aagaagctct	240
atataaatcc aagacaagca acaaaccctt gatgattatt catcacttgg atgagtgcc	300
acacagtcna gctttaaaga aagtgtttgc tgaaaataaa gaaatccaga aattggcaga	360
gcagtttgtc ctctcaatc tggtttatga aacaactgac aaacaccttt ctctgatgg	420
ccagtatgtc ccaggattat gttgttgac ccatctctga cagttgaagc cgatatcctg	480
ggaagatatt cnaaccgtct ctatgcttac aaactgcaga tacgctctgt tgcttgacac	540
atgaaaaagc tctcaagttg ctnaaaatga attgtgaaga aaaaaatctc cagccttctg	600
tctgtcggct tgaaaattga aaccagaaaa atgtgaaaaa tggctattgt ggaacanatn	660
gacacctgat taggttttgg ttatgttcac cactattttt aanaaaanan nttttaaaat	720
ttggttcaat tntctttttt aaacaatntg tttctacntt gnganctgat ttctaaaaaa	780
aataatnttt ggc	793

<210> 79

<211> 456

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(456)
 <223> n = A,T,C or G

<400> 79

actagtatgg ggtgggaggc cccacccttc tcccctagge gctgttcttg ctccaaaggg	60
ctccgtggag agggactggc agagctgang ccacctgggg ctggggatcc cactcttctt	120
gcagctgttg agcgaccta accactgggt atgccccac cctgtcttc cgcacccgct	180
tcctcccgac cccangacca ggctacttct cccctcctct tgccctccctc ctgccccctgc	240
tgccctgat cgtangaatt gangantgtc ccgccttggt gctganaatg gacagtggca	300
ggggctggaa atgggtgtgt gtgtgtgtgt gtgtgtgtgt gtgtgtgtgt gnccccccc	360
tgcaagaccg agattgagg aaancatgtc tgctgggtgt gaccatgttt cctctccata	420
aantnccct gtgacnctca naaaaaaaaa aaaaaa	456

<210> 80
 <211> 284
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(284)
 <223> n = A,T,C or G

<400> 80

ctttgtacct ctgaaaaaga taggtattgt gtcataaaac ttgagtttaa attttatata	60
taaaactaaa agtaatgtc actttagcaa cacatactaa aattggaacc atactgagaa	120
gaatagcatg acctccgtgc aaacaggaca agcaaatttg tgatgtgttg attaaaaaga	180
aataaataaa tgtgtatatg tgtaacttgt atgtttatgt ggaatacaga ttgggaaata	240
aatgtattt cttactgtga aaaaaaaaaa aaaaaaaaaa aana	284

<210> 81
 <211> 671
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(671)
 <223> n = A,T,C or G

<400> 81

gccaccaaca ttccaagcta ccctgggtac ctttgtgcag tagaagctag tgagcatgtg	60
agcaagcggg gtgcacacgg agactcatcg ttataattta ctatctgcc aagtagagaa	120
gaaaggctgg ggatatttgg gttggcttgg ttttgatttt ttgcttgttt gtttgtttt	180
tactaaaaca gtattatctt ttgaatateg tagggacata agtatataca tgttatccaa	240
tcaagatggc tagaatggtg cctttctgag tgcataaaac ttgacacccc tggtaaactc	300
ttcaacacac ttccactgcc tgogtaatga agttttgatt catttttaac cactggaatt	360
tttcattgac gtcattttca gttagatnat ttgacattt gagattaaaa tgccatgtct	420
atttgattag tcttattttt ttatttttac aggcattatca gtctcactgt tggctgtcat	480
tgtagacaaag tcaataaaac ccccnaggac aacacacagt atgggatcac atattgtttg	540
acattaagct ttggccaaaa aatgttgcac gtgttttacc tcgacttgct aaatcaatan	600
canaaaggct ggctnataat gttggtggtg aaataattaa tnantaacca aaaaaaaaaa	660
aaaaaaaaa a	671

<210> 82
 <211> 217
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(217)
 <223> n = A,T,C or G

<400> 82
 ctgcagatgt ttcttgaatg ctttgtcaaa ttaanaaagt taaagtgcaa taatgtttga 60
 agacaataag tgggtgtgta tcttgtttct aataagataa acttttttgt ctttgcttta 120
 tcttattagg gagggtgatg tcagtgtata aaacatactg tgttgtataa caggcttaat 180
 aaattcttta aaaggaaaaa aaaaaaaaaa aaaaaaa 217

<210> 83
 <211> 460
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(460)
 <223> n = A,T,C or G

<400> 83
 cgcgagtggg agcaccagga tctcgggctc ggaacgagac tgcacggatt gttttaagaa 60
 aatggcagac aaaccagaca tgggggaaat cgccagcttc gatnaggcca agctgaanaa 120
 aacggagacg caggagaaga acaccctgcc gaccaaagag accattgagc angagaagcg 180
 gagtgaatt tcctaagatc ctggaggatt tcctaccccc gtctctctcg agacccagct 240
 cgtgatgtgg aggaagagcc acctgcaaga tggacacgag ccacaagctg cactgtgaac 300
 ctgggcactc cgcgccgatg ccaccggcct gtgggtctct gaagggaccc cccccaatcg 360
 gactgcaaaa ttctccggtt tgccccggga tattatacaa nattatttgt atgaataatg 420
 annataaaac acacctcgtg gcancaaana aaaaaaaaaa 460

<210> 84
 <211> 323
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(323)
 <223> n = A,T,C or G

<400> 84
 tgggtgatct tggctctgtg gagctgctgg gacgggatct aaaagactat tctggaagct 60
 gtggtccaan gcattttgct ggcttaacgg gtcccggaac aaaggacacc agctctctaa 120
 aattgaagtt taccoganat aacaatcttt tgggcagaga tgcctatatt aacaaacncc 180
 gtccctgcgc aacaacnaac aatctctggg aaatacggc catgaacntg ctgtctcaat 240
 cnancatctc tctagctgac cgatcatatc gtcccagatt actacanatc ataataattg 300
 atttctctgta naaaaaaaaaa aaa 323

<210> 85
 <211> 771
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(771)
 <223> n = A,T,C or G

<400> 85
 aaactgggta ctcaacactg agcagatctg ttctttgagc taaaaacat gtgctgtacc 60
 aanagtttgc tcctggctgc tttgatgtca gtgctgtac tccacctctg cggcgaatca 120
 gaagcaagca actttgactg ctgtcttgga tacacagacc gtattcttca tcctaaattt 180
 attgtgggct tcacacggca gctggccaat gaaggctgtg acatcaatgc tatcatcttt 240
 cacacaaaga aaaagttgtc tgtgtgcgca aatccaaaac agacttgggt gaaatatatt 300
 gtgctgtctc tcagtaaaaa agtcaagaac atgtaaaaac tgtggctttt ctggaatgga 360
 attggacata gccaagaac agaaagaact tgctggggtt ggagggttca cttgcacatc 420
 atgganggtt tagtgettat cttatttgtg cctcctggac ttgtccaatt natgaagtta 480
 atcatattgc atcatanttt gctttgttta acatcacatt naaattaaac tgtattttat 540
 gttattttata gctntaggtt ttctgtgttt aactttttat acnaantttc cttaaactatt 600
 ttggtntant gcaanttaaa aatttatattt ggggggggaa taaatattgg antttctgca 660
 gccacaagct ttttttaaaa aaccantaca nccnngttaa atggtnngtc ccnaatgggt 720
 tttgcttttn antagaaaat ttnttagaac natttgaaaa aaaaaaaaaa a 771

<210> 86
 <211> 628
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(628)
 <223> n = A,T,C or G

<400> 86
 actagtttgc tttacatttt tgaaaagtat tatttttgtc caagtgttta tcaactaaac 60
 cttgtgttag gtaagaatgg aatttattaa gtgaatcagt gtgaccttc ttgtcataag 120
 attatcttaa agctgaagcc aaaatatgct tcaaaagaaa angactttat tgttcattgt 180
 agttcataca ttcaaagcat ctgaactgta gtttctatag caagccaatt acatccataa 240
 gtggagaang aaatagatta atgtcnaagt atgattgggtg gagggagcaa ggttgaagat 300
 aatctgggggt tgaaattttc tagttttcat tctgtacatt tttagttna catcagattt 360
 gaaatattaa tgtttacctt tcaatgtgtg gtatcagctg gactcantaa cacccttctc 420
 ttccctnngg gatggggaat ggattattgg aaaatggaaa gaaaaaagta cttaaagcct 480
 tcctttcnca gtttctggct cctacctac tgatttancc agaataagaa aacattttat 540
 catcntctgc tttattccca ttaatnaant tttgatgaat aaatctgctt ttatgcnnac 600
 ccaaggaatt nagtggnttc ntcttgt 628

<210> 87
 <211> 518
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature

<222> (1)... (518)

<223> n = A,T,C or G

<400> 87

ttttttattt	tttttagaga	gtagttcagc	ttttatttat	aaatttattg	cctgttttat	60
tataacaaca	ttatactgtt	tatggtttaa	tacatatggg	tcaaaatgta	taatacatca	120
agtagtacag	ttttaaaatt	ttatgcttaa	aacaagtttt	gtgtaaaaaa	tgtagatata	180
ttttacatgg	caaatcaatt	tttaagtcac	cctaaaaatt	gatttttttt	tgaaatttaa	240
aaacacattt	aatttcaatt	tctctcttat	ataaccttta	ttactatagc	atggtttcca	300
ctacagttta	acaatgcagc	aaaattccca	tttcacggta	aattgggttt	taagcggcaa	360
ggttaaaatg	ctttgaggat	cctnaatacc	ctttgaactt	caaatgaagg	ttatggttgt	420
naatttaacc	ctcatgccat	aagcagaagc	acaagtttag	ctgcattttg	ctctaaactg	480
taaaancgag	ccccccgttg	aaaaagcaaa	agggaccc			518

<210> 88

<211> 1844

<212> DNA

<213> Homo sapien

<400> 88

gagacagtga	atcctagtat	caaaggattt	ttggcctcag	aaaaagttgt	tgattatttt	60
tattttattt	tatttttoga	gactcgtct	caaaaaaaaa	aaaaaaaaaa	agaatcacia	120
ggtagttgct	aaagcatttt	gagctgcttg	gaaaaaggga	agtagttgca	gtagagtttc	180
ttccatcttc	ttgggtgctg	gaagccatat	atgtgtcttt	tactcaagct	aaggggtata	240
agcttatgtg	ttgaatttgc	tacatctata	tttcacatat	tctcacaata	agagaatttt	300
gaaatagaaa	tatcatagaa	catttaagaa	agtttagtat	aaataatatt	ttgtgtgttt	360
taatcccttt	gaagggatct	atccaaagaa	aatattttac	actgagctcc	ttcctacacg	420
tctcagtaac	agatcctgtg	ttagtctttg	aaaatagctc	atttttttaa	tgtagtgag	480
tagatgtagc	atacatatga	tgtataatga	cgtgtattat	gttaacaatg	tctgcagatt	540
ttgtaggaat	acaaaacatg	gcctttttta	taagcaaaac	gggccaatga	ctagaataac	600
acatagggca	atctgtgaat	atgtattata	agcagcattc	cagaaaagta	gttgggtgaa	660
taattttcaa	gtcaaaaagg	gatatggaaa	gggaattatg	agtaacctct	attttttaag	720
ccttgctttt	aaattaaacg	ctacagccat	tttaagccttg	aggataataa	agcttgagag	780
taataatgtt	aggttagcaa	aggttttagat	gtatcacttc	atgcagtcta	ccatgatagt	840
aatgcagctc	ttogagtcac	ttctgggtcat	tcaagatatt	cacccttttg	cccatagaaa	900
gcaccctacc	tcacctgctt	actgacattg	tcttagctga	tcacaagatc	attatcagcc	960
tccattattc	cttactgtat	ataaaataca	gagttttata	ttttcctttc	ttogtttttc	1020
accatattca	aaacctaaat	ttgtttttgc	agatggaatg	caaagtaatc	aagtgttcgt	1080
gctttcacct	agaaggggtg	ggctcctgaag	gaaagagggtc	cctaaatatc	ccccaccctg	1140
gggtgctcctc	cttccctggg	accctgacta	ccagaagtca	gggtgctagag	cagctggaga	1200
agtgccagcag	cctgtgcttc	cacagatggg	gggtgctgctg	caacaaggct	ttcaatgtgc	1260
ccatcttagg	gggagaagct	agatcctgtg	cagcagcctg	gtaagtcctg	aggaggttcc	1320
attgctcttc	ctgctgctgt	cctttgcttc	tcaacggggc	tcgctctaca	gtctagagca	1380
catgcagcta	acttgtgcct	ctgcttatgc	atgaggggta	aattaacaac	cataaccttc	1440
atttgaagtt	caaaggtgta	ttcaggatcc	tcaaagcatt	ttaaccttgc	cgcttaaaac	1500
ccaattttacc	gtgaaatggg	aattttgctg	cattgtttaa	ctgtagtgga	aacctgcta	1560
tagaataaaa	ggttatataa	gagagaaatt	gaaattaaat	gtgtttttta	atttcaaaaa	1620
aaaatcaatc	tttaggatga	cttaaaaatt	gatttgccat	gtaaaatgta	tctgcatttt	1680
ttacacaaaa	cttgttttta	gcataaaatt	ttaaaactgt	actacttgat	gtattataca	1740
ttttgaacca	tatgtattaa	accataaaca	gtataatgtt	gttataataa	aacagggaat	1800
aaattttataa	ataaaagctg	aaaaaaaaaa	aaaaaaaaaa	aaaa		1844

<210> 89

<211> 523

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(523)

<223> n = A,T,C or G

<400> 89

tttttttttt	tttttttagt	caatccacat	ttattgatca	cttattatgt	accaggcact	60
gggataaaga	tgactgtag	tcactcacag	taaggaagaa	aactagcaaa	taagacgatt	120
acaatatgat	gtagaaaatg	ctaagccaga	gatatagaaa	ggtcctattg	ggtccttctg	180
tcaccttgtc	tttcacatc	cctacccttc	acaggccttc	cctccagctt	cctgcccccg	240
ctccccactg	cagatccctt	gggattttgc	ctagagctaa	acgagganat	gggccccctg	300
gccctggcat	gacttgaacc	caaccacaga	ctgggaaagg	gagcctttcg	anagtggatc	360
actttgatna	gaaaacacat	aggggaattga	agagaaantc	cccaaattggc	caccctgtgt	420
ggtgctcaag	aaaagtgtgc	agaatggata	aatgaaggat	caagggaatt	aatanaatgaa	480
taattgaatg	gtggctcaat	aagaatgact	ncnttgaatg	acc		523

<210> 90

<211> 604

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(604)

<223> n = A,T,C or G

<400> 90

ccagtgtggt	ggaatgcaaa	gattaccccg	gaagctttcg	agaagctggg	attccctgca	60
gcaaaggaaa	tagccaatat	gtgtcggttc	tatgaaatga	agccagaccg	agatgtcaat	120
ctcaccacc	aactaaatcc	caaagtcaaa	agcttcagcc	agtttatctc	agagaaccag	180
gggagccttc	aagggcatgt	agaaaatcag	ctgttcagat	aggcctctgc	accacacagc	240
ctctttcttc	tctgatecct	ttcctcttta	cggcacaaca	ttcatgtttg	acagaacatg	300
ctggaatgca	attgtttgca	acaccgaagg	atttcctgcy	gtgcctctt	cagtaggaag	360
cactgcattg	gtgataggac	acggtaattt	gattcacatt	taacttgcta	gttagtgata	420
aggggtggta	cacctgtttg	gtaaaatgag	aagcctcgga	aacttgggag	cttctctcct	480
accactaatg	gggagggcag	attattactg	ggattttctc	tggggtgaat	taatttcaag	540
ccctaattgc	tgaaattccc	ctnggcaggc	tccagttttc	tcaactgcat	tgcaaaattc	600
cccc						604

<210> 91

<211> 858

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(858)

<223> n = A,T,C or G

<400> 91

tttttttttt	ttttttttta	tgattattat	tttttttatt	gatctttaca	tcctcagtgt	60
tggcagagtt	tctgatgctt	aataaacatt	tgttctgac	agataagtgg	aaaaaattgt	120
catttccctta	ttcaagccat	gcttttctgt	gatattctga	tcctagtgtg	acatacagaa	180

ataaatgtct	aaaacagcac	ctcgattctc	gtctataaca	ggactaagtt	cactgtgatc	240
ttaaataagc	ttggctaaaa	tgggacatga	gtggaggtag	tcacacttca	gcgaagaaag	300
agaatctcct	gtataatctc	accaggagat	tcaacgaatt	ccaccacact	ggactagtgg	360
atcccccggg	ctgcaggaat	tcgatatcaa	gcttatcgat	accgtcgacc	tcgagggggg	420
gccccgtacc	caattcgccc	tatagtgagt	cgtattacgc	gcgctcactg	gcgctcgttt	480
tacaaactcg	tgactgggaa	aaccctggcg	ttaccctaact	taatcgctt	gcagcacatc	540
cccctttcgc	cagctggcgt	aatagcgaa	agcccgacc	gatcgccctt	ncaacagttg	600
cgcagcctga	atggcgaaatg	ggacgcgccc	tgtagcggcg	cattaaagcg	cggcnggggtg	660
tggnggntcc	cccacgtgac	cgntacactt	ggcagcgccct	tacgcgggtc	nttcgctttc	720
ttcccttctt	ttctcgacc	gttcgcgggg	tttccccggn	agctnttaat	cgggggnctc	780
cctttanggg	tncnaattaa	nggnttacng	gaccttngan	cccaaaaact	ttgattaggg	840
ggaaggtccc	cgaagggg					858

<210> 92

<211> 585

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (585)

<223> n = A,T,C or G

<400> 92

gttgaatctc	ctgggtgagat	tatacaggag	attctctttc	ttcgtgaag	tgtgactacc	60
tccactcatg	tcccatttta	gccaagctta	tttaagatca	cagtgaactt	agtcctgtta	120
tagacgagaa	tcgaggtgct	gttttagaca	tttatttctg	tatgttcaac	taggatcaga	180
atatcacaga	aaagcatggc	ttgaataagg	aaatgacaat	tttttccact	tatctgatca	240
gaacaaatgt	ttattaagca	tcagaaactc	tgccaacact	gaggatgtaa	agatcaataa	300
aaaaaataat	aatcatnann	naaanannan	nngaagggcg	gccgccaccg	cgggtggagct	360
ccagcttttg	ttcccttttag	tgaggggttaa	ttgcgcgctt	ggcggttaatc	atgggtcatag	420
ctgtttcctg	tgtgaaattg	ttatccggct	cacaattccn	cncaacatac	gagccgggaa	480
gcntnangtg	taaaagcctg	gggggtgccta	attgagttag	ctnactcaca	ttaattgngt	540
tgcgtccac	ttgccgcgtt	ttccantccg	ggaaacctgt	tcgnc		585

<210> 93

<211> 567

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (567)

<223> n = A,T,C or G

<400> 93

cggcagtgtt	gctgtctgcg	tgtccacctt	ggaatctggc	tgaactggct	gggaggacca	60
agactgcggc	tgggggtggc	anggaaggga	accgggggct	gctgtgaagg	atcttggaac	120
ttccctgtac	ccaccttccc	cttgcttcat	gtttgtanag	gaaccttgtg	ccggccaagc	180
ccagtttctt	tgtgtgatac	actaatgtat	ttgctttttt	tgggaaatan	anaaaaaatca	240
attaaattgc	tantgtttct	ttgaannnnn	nnnnnnnnnn	nnnnnnnggg	ggggncgccc	300
ccnccgngga	aacnccccct	tttgttccct	ttaattgaaa	ggtaattng	cncnctggc	360
gttaancnt	gggccaaanc	tngttneccg	tgntgaaatt	gttnatcccc	tcccaaattc	420
ccccccnncc	ttccaaaccc	ggaaancctn	annntgttna	ancccggggg	gttgccctaan	480
ngnaattnaa	ccnaaccccc	ntttaaatng	nnnttgcn	ccacnngccc	cnctttccca	540

nttcggggaa aacctntcc gtgccca

567

<210> 94
 <211> 620
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)... (620)
 <223> n = A,T,C or G

<400> 94
 actagtcaaa aatgctaaaa taatttggga gaaaatattt ttttaagtagt gttatagttt 60
 catgtttatc ttttattatg ttttgtgaag ttgtgtcttt tcactaatta cctatactat 120
 gccaatattt ccttatatct atccataaca tttatactac atttgaana naatatgcac 180
 gtgaaactta acactttata aggtaaaaat gaggtttcca anatttaata atctgatcaa 240
 gttcttggtta tttccaaata gaatggactt ggtctgttaa gggctaagga gaagaggaag 300
 ataagggttaa aagtgtgtaa tgaccaaaca ttctaaaaga aatgcaaaaa aaaagtttat 360
 tttcaagcct tcgaactatt taaggaaagc aaaatcattt cctaaatgca tatcatttgt 420
 gagaatttct cattaatatc ctgaatcatt catttcacta aggctcatgt tnactccgat 480
 atgtctctaa gaaagtacta tttcatggtc caaacctggt tgccatantt gggtaaaggc 540
 tttcccttaa gtgtgaaant atttaaaatg aaattttcct ctttttaaaa attctttana 600
 aggggttaagg gtgttgggga 620

<210> 95
 <211> 470
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)... (470)
 <223> n = A,T,C or G

<400> 95
 ctcgaccttc tctgcacagc ggatgaacct tgagcagctg aagaccagaa aagccactat 60
 nactttntgc ttaattcang agcttacang attcttcaaa gagtgngtcc agcatccttt 120
 gaaacatgag ttcttaccag cagaagcaga cctttacccc accacctcag cttcaacagc 180
 agcaggtgaa acaaccatc cagcctccac ctnaggaaat atttgttccc acaaccaagg 240
 agccatgcca ctcaaagggt ccacaacctg naaacacaaa nattccagag ccagggtgta 300
 ccaagggtccc tgagccaggg ctgtaccaan gtccctgagc cagggtgtac caangtcctt 360
 gagccaggat gtaccaagggt ccctgancca ggttgtccaa ggtccctgag ccagggtaca 420
 ccaagggcct gngccaggca gcatcaangt ccttgaccaa ggcttatcaa 470

<210> 96
 <211> 660
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)... (660)
 <223> n = A,T,C or G

<400> 96

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gcattttcttt	tcatttgaat	cttcagatga	accctgagca	gccgaagacc	agaaaagcca	120
tgaagacttt	ctgcttaatt	caggggctta	caggattctt	cagagtgtgt	gtgaacaaaa	180
gctttatagt	acgtattttt	aggatacaaa	taagagagag	actatggctt	ggggtgagaa	240
tgtactgatt	acaaggtcta	cagacaatta	agacacagaa	acagatggga	agaggggtgnc	300
cagcatctgg	nggttggctt	ctcaagggct	tgtctgtgca	ccaaattact	tctgcttggn	360
cttctgctga	gctgggcctg	gagtgaccgt	tgaaggacat	ggctctggta	cctttgtgta	420
gcctgncaca	ggaactttgg	tgtatccttg	ctcagggaact	ttgatggcac	ctggctcagg	480
aaacttgatg	aagccttgg	caagggacct	tgatgcttgc	tggctcaggg	accttggngn	540
ancctgggct	canggacctt	tgncicaacc	ttggcttcaa	gggaccttg	gnacatcctg	600
gcnnagggac	ccttgggncc	aacctggggc	tnaggggacc	ctttggntnc	nanccttggc	660

<210> 97

<211> 441

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(441)

<223> n = A,T,C or G

<400> 97

gggaccatac	anagtattcc	tctcttcaca	ccaggaccag	ccactgttgc	agcatgagtt	60
cccagcagca	gaagcagccc	tgcattccac	cccctcagct	tcagcagcag	cagggtgaac	120
agccttgcca	gcctccacct	caggaaccat	gcattcccaa	aaccaaggag	ccctgccacc	180
ccaaggtgcc	tgagccctgc	caccccaaag	tgcttgagcc	ctgccagccc	aaggttccag	240
agccatgcca	ccccaaggtg	cctgagccct	gcccttcaat	agtcaactcca	gcaccagccc	300
agcagaanac	caagcagaag	taatgtggtc	cacagccatg	cccttgagga	gccggccacc	360
agatgctgaa	tccctatcc	cattctgtgt	atgagtccca	tttgccctgc	aattagcatt	420
ctgtctcccc	caaaaaaaaa	a				441

<210> 98

<211> 600

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(600)

<223> n = A,T,C or G

<400> 98

gtattcctct	cttcacacca	ggaccagcca	ctgttgagc	atgagttccc	agcagcagaa	60
gcagccctgc	atcccacccc	ctcagcttca	gcagcagcag	gtgaaacagc	cttgccagcc	120
tccacctcag	gaacctgca	tccccaaaac	caaggagccc	tgccacccc	aggtgacctga	180
gcctgtccac	cccaaagtgc	ctgagccctg	ccagcccaag	gttccagagc	catgccaccc	240
caaggtgcct	gagccctgcc	cttcaatagt	cactccagca	ccagcccagc	agaanaccaa	300
gcagaagtaa	tgtggtccac	agccatgccc	ttgaggagcc	ggccaccana	tgctgaatcc	360
cctatcccat	tctgtgtatg	agtcacattt	gccttgcaat	tagcattctg	tctcccccaa	420
aaaagaatgt	gctatgaagc	tttctttcct	acacactctg	agtctctgaa	tgaagctgaa	480
ggtcttaant	acaganctag	ttttcagctg	ctcagaattc	tctgaagaaa	agatttaaga	540
tgaaaggcaa	atgattcagc	tccttattac	ccattaaat	tcnctttcaa	ttccaaaaaa	600

<210> 99
 <211> 667
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1) ... (667)
 <223> n = A,T,C or G

<400> 99
 actagtgact gagttcctgg caaagaaatt tgacctggac cagttgataa ctcattgtttt 60
 accattttaa aaaatcagt aaggatttga gctgctcaat tcaggacaaa gcattcgaac 120
 ggtcctgacg ttttgagatc caaagtggca ggaggtctgt gttgtcatgg tgaactggag 180
 tttctcttgt gagagttccc tcatctgaaa tcatgtatct gtctcaciaa tacaagcata 240
 agtgaagat ttgttgaaga catagaaccc ttataaagaa ttattaacct ttataaacat 300
 tttaaagtctt gtgagcacct gggaattagt ataataacaa tgttnatatt tttgatttac 360
 attttgtaag gctataattg tatcttttaa gaaaacatac cttggatttc tatgttgaaa 420
 tggagatttt taagagtttt aaccagctgc tgcagatata ttactcaaaa cagatatagc 480
 gtataaagat atagtaaag catctcctag agtaatatc acttaacaca ttggaaacta 540
 ttatttttta gatttgaata tnaatgttat tttttaaaca cttgttatga gttacttggg 600
 attacatttt gaaatcagtt cattccatga tgcanattac tgggattaga ttaagaaaga 660
 cggaaaaa 667

<210> 100
 <211> 583
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1) ... (583)
 <223> n = A,T,C or G

<400> 100
 gttttgtttg taagatgatc acagtcattg tacactgatc taaaggacat atatataacc 60
 ctttaaaaaa aaaatcactg cctcattctt atttcaagat gaatttctat acagactaga 120
 tgtttttctg aagatcaatt agacattttg aaaatgattt aaagtgtttt ctttaatgtt 180
 ctctgaaaac aagtttcttt ttagtattta accaaaaaag tgcccttttt gtcactggat 240
 tctcctagca ttcattgattt ttttttcata caatgaaatt aaaattgcta aaatcatgga 300
 ctggctttct ggttggattt caggtaagat gtgtttaagg ccagagcttt tctcagtatt 360
 tgattttttt cccaatatt tgatttttta aaaatatata catnggtgct gcatttatat 420
 ctgctggttt aaaattctgt catatttcac ttctagcctt ttagttatgg caaatcatat 480
 ttacttttta cttaaagcat ttggttnattt ggantatctg gttctannct aaaaaanta 540
 attctatnaa ttgaantttt ggtactcnnc catatttggg tcc 583

<210> 101
 <211> 592
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1) ... (592)
 <223> n = A,T,C or G

<400> 101

gtggagacgt	acaaagagca	gccgctcaag	acacctggga	agaaaaagaa	aggcaagccc	60
gggaaacgca	aggagcagga	aaagaaaaaa	cggcgaactc	gctctgcctg	gtagactct	120
ggagtgactg	ggagtgggct	agaaggggac	cacctgtctg	acacctccac	aacgtcgctg	180
gagctcgatt	cacggaggca	ttgaaatttt	cagcaganac	cttccaagga	catattgcag	240
gattctgtaa	tagtgaacat	atggaaaagta	ttagaaatat	ttattgtctg	taaatactgt	300
aaatgcattg	gaataaaaact	gtctccccc	ttgctctatg	aaactgcaca	ttggtcattg	360
tgaatatttt	tttttttgcc	aaggctaata	caattattat	tatcacattt	accataattt	420
attttgtcca	ttgatgtatt	tattttgtaa	atgtatcttg	gtgctgctga	atttctatat	480
tttttgtaca	taatgcnttt	anatatacct	atcaagtttg	ttgataaatg	acncaatgaa	540
gtgncncnan	ttgngggtg	aatttaatga	atgcctaatt	ttattatccc	aa	592

<210> 102

<211> 587

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (587)

<223> n = A,T,C or G

<400> 102

cgctcctaagc	acttagacta	catcagggaa	gaacacagac	cacatccctg	tcctcatgcg	60
gcttatgttt	tctggaagaa	agtggagacc	nagtccttgg	ctttagggct	ccccggctgg	120
gggtgtgca	ntccggtcag	ggcgggaagg	gaaatgcacc	gctgcatgtg	aacttacagc	180
ccaggcggat	gcccttccc	ttagcactac	ctggcctcct	gcateccctc	gcctcatgtt	240
cctcccacct	tcaaanaatg	aanaacccca	tgggccagc	cccttgccct	ggggaaccaa	300
ggcagccttc	caaaactcag	gggctgaagc	anactattag	ggcaggggct	gactttgggt	360
gacactgccc	attccctctc	agggcagctc	angtcacccn	ggncctctga	accagcctg	420
ttcctttgaa	aaagggcaaa	actgaaaagg	gcttttccta	naaaaagaaa	aaccagggaa	480
ctttgccagg	gcttcnntnt	taccaaaacn	ncttctcnng	gatttttaat	tccccattng	540
gcctccactt	accnggggcn	atgccccaaa	attaanaatt	tcccatc		587

<210> 103

<211> 496

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (496)

<223> n = A,T,C or G

<400> 103

anaggactgg	ccctacntgc	tctctctcgt	cctacctatc	aatgccaac	atggcagaac	60
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gcggtgggtc	tccaccacaa	ccactttgac	tctgtggtcc	ctgnanggtg	gnttctcctg	180
actggcagga	tggaccttan	ccnacatata	cctctgttcc	ctctgctnag	anaaagaatt	240
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ttgcctacag	aatttcattc	agtctacact	ttggcattct	ctctggcgat	agagtgtggc	360
tgggctgacc	gcaaaagggtg	ccttacacac	tggcccccac	cctcaaccgt	tgacncatca	420
gangcttgcc	tcctccttct	gattnncccc	catgttggat	atcagggtgc	tcnagggtt	480
ggaaaagaaa	caaaac					496

<210> 104
 <211> 575
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1) ... (575)
 <223> n = A,T,C or G

<400> 104		
gcacctgctc tcaatccnnc tctcaccatg atcctccgcc tgcanaaact cctctgccaa		60
ctatggangt ggtttcnggg gtggctcttg ccaactggga agaagccgtg gtgtctctac		120
ctgttcaact cngtttgtgt ctgggggatc aactnngggc tatggaagcg gctnaactgt		180
tgttttggtg gaagggctgg taattggctt tgggaagtng cttatngaag ttggcctngg		240
gaagttgcta ttgaaagtng ccntggaaagt ngntttggtg gggggttttg ctggtggcct		300
ttgttnaatt tgggtgcttt gtnaatggcg gccccctcnc ctgggcaatg aaaaaaatca		360
ccnatgcngn aaacctcnac nnaacagcct gggcttcctt cacctcgaaa aaagttgctc		420
cccccccaaa aaaggncaan cccctcaann tggaangttg aaaaaatcct cgaatgggga		480
nccnnaaac aaaaancccc ccntttcccn gnaanggggg aaataaccnc cccccactta		540
cnaaaaccct tntaaaaaac cccccgggaa aaaaa		575

<210> 105
 <211> 619
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1) ... (619)
 <223> n = A,T,C or G

<400> 105		
cactagtagg atagaaacac tgtgtcccgag gagtaaggag agaagctact attgattaga		60
gcctaaccce ggtaactgc aagaagaggc gggatacttt cagctttcca tgtaactgta		120
tgcataaagc caatgtagtc cagtttctaa gatcatgttc caagctaact gaatcccat		180
tcaatacaca ctcatgaact cctgatggaa caataacagg cccaagcctg tggtagatg		240
tgcacacttg ctagactcan aaaaaatact actctcataa atgggtggga gtattttggt		300
gacaacctac tttgcttggc tgagtgaagg aatgatattc atatattcat ttattccatg		360
gacatttagt tagtgctttt tatataccag gcatgatget gagtgacact cttgtgtata		420
tttccaaatt tttgtacagt cgctgcacat atttgaaatc atatattaag acttccaaaa		480
aatgaagtcc ctggtttttc atggcaactt gatcagtaaa ggattcncct ctggttggtg		540
cttaaaacat ctactatatn gttanatatga aattcctttt ccccnctcc cgaaaaaana		600
aagtgggtggg gaaaaaaaa		619

<210> 106
 <211> 506
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1) ... (506)
 <223> n = A,T,C or G

<400> 106

cattggtnct	ttcatttgct	ntggaagtgt	nmatctctaa	cagtggacaa	agttcccngt	60
gccttaaact	ctgtnacact	tttggaant	gaaaantng	tantatgata	ggttattctg	120
angtanagat	gttctggata	ccattanatn	tgccccngt	gtcagaggct	catattgtgt	180
tatgtaaag	gtatntcatt	cgctactatn	antcaatng	aaatanggtc	tttgggttat	240
gaatantng	cagcncanct	nanangctgt	ctgtngtatt	cattgtggtc	atagcacctc	300
acancattgt	aacctcnatc	nagtggagaca	nactagnaant	ttcctagtga	tggctcanga	360
ttccaaatgg	netcatntcn	aatgtttaaa	agttanttaa	gtgtaagaaa	tacagactgg	420
atgttccacc	aactagtacc	tgtaatgacn	ggcctgtccc	aacacatctc	ccttttccat	480
gactgtggta	ncccgcatcg	gaaaaa				506

<210> 107

<211> 452

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (452)

<223> n = A,T,C or G

<400> 107

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tcttttgaag	catagataat	attgtttggg	aaatgtttct	tttgtttggg	aaatgtttct	120
tttaaagacc	ctectattct	ataaaactct	gcatgtagag	gcttgtttac	ccttctctct	180
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tggaaagtaa	ctgtganaac	ccagtttccc	gtccatctcc	cttagggact	acccatagaa	360
catgaaaagg	tccccacnga	agcaagaaga	taagtctttc	atggctgctg	gttgcttaaa	420
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<210> 108

<211> 502

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (502)

<223> n = A,T,C or G

<400> 108

atcttcttcc	cttaattagt	tnttatttat	ntattaaatt	ttattgcatg	tcttggaaca	60
caaaaagaga	ttgtagattg	gcttctggct	ccccaaaagc	ccataacaga	aagtaccaca	120
agaccncaac	tgaagcttaa	aaaatctatc	acatgtataa	tacctttnga	agaacattaa	180
tanagcatat	aaaactttta	acatntgctt	aatgttgtnc	aattataaaa	ntaatngaaa	240
aaaatgtccc	tttaacatnc	aatatcccac	atagtgttat	ttnaggggat	taccnngnaa	300
naaaaaaagg	gtagaaggga	tttaatgaaa	actctgcttn	ccatttctgt	ttanaaacgt	360
ctccagaaca	aaaacttntc	aantctttca	gctaaccgca	tttgagctna	ggccactcaa	420
aaactccatt	agncccactt	tctaanggtc	tctanagctt	actaancctt	ttgaccctt	480
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<210> 109

<211> 1308

<212> DNA

<213> Homo sapien

<400> 109

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ggcatcttga ctgcaattgg catggctctc ctggggaccc gaggagccac cgcttcccag      180
ttggaggagg tgtttctactc tgaaaaagag acgaagagct caagaataaa ggctgaagaa      240
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ataagcaaac tctaataatga ttatgaactg aacataacca acaggtctgt tggagaaaaa      360
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gaacctgttg attttgtaaa tgcagccgat gaaagtcgaa agaagattaa ttcttgggtt      480
gaaagcaaaa caaatgaaaa aatcaaggac ttgttcccag atggctctat tagtagctct      540
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gatggcctgg agaagataat agataaaata agtcttgaga aattggtaga gtggactagt      840
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tttactgtca catcggcccc aggtcatgaa aatgttcaact gcaatcatcc cttcctgttc      1140
ttcatcaggc acaatgaatc caacgacatc ctcttcttcg gcagattttc ttctccttaa      1200
gatgategtt gccatggcat tgctgctttt agcaaaaaac aactaccagt gttactcata      1260
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<210> 110

<211> 391

<212> PRT

<213> Homo sapien

<400> 110

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          20          25          30
Gly Ile Leu Thr Ala Ile Gly Met Val Leu Leu Gly Thr Arg Gly Ala
          35          40          45
Thr Ala Ser Gln Leu Glu Glu Val Phe His Ser Glu Lys Glu Thr Lys
          50          55          60
Ser Ser Arg Ile Lys Ala Glu Glu Lys Glu Val Ile Glu Asn Thr Glu
          65          70          75          80
Ala Val His Gln Gln Phe Gln Lys Phe Leu Thr Glu Ile Ser Lys Leu
          85          90          95
Thr Asn Asp Tyr Glu Leu Asn Ile Thr Asn Arg Leu Phe Gly Glu Lys
          100          105          110
Thr Tyr Leu Phe Leu Gln Lys Tyr Leu Asp Tyr Val Glu Lys Tyr Tyr
          115          120          125
His Ala Ser Leu Glu Pro Val Asp Phe Val Asn Ala Ala Asp Glu Ser
          130          135          140
Arg Lys Lys Ile Asn Ser Trp Val Glu Ser Lys Thr Asn Glu Lys Ile
          145          150          155          160
Lys Asp Leu Phe Pro Asp Gly Ser Ile Ser Ser Ser Thr Lys Leu Val
          165          170          175

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Leu Val Asn Met Val Tyr Phe Lys Gly Gln Trp Asp Arg Glu Phe Lys
 180 185 190
 Lys Glu Asn Thr Lys Glu Glu Lys Phe Trp Met Asn Lys Ser Thr Ser
 195 200 205
 Lys Ser Val Gln Met Met Thr Gln Ser His Ser Phe Ser Phe Thr Phe
 210 215 220
 Leu Glu Asp Leu Gln Ala Lys Ile Leu Gly Ile Pro Tyr Lys Asn Asn
 225 230 235 240
 Asp Leu Ser Met Phe Val Leu Leu Pro Asn Asp Ile Asp Gly Leu Glu
 245 250 255
 Lys Ile Ile Asp Lys Ile Ser Pro Glu Lys Leu Val Glu Trp Thr Ser
 260 265 270
 Pro Gly His Met Glu Glu Arg Lys Val Asn Leu His Leu Pro Arg Phe
 275 280 285
 Glu Val Glu Asp Ser Tyr Asp Leu Glu Ala Val Leu Ala Ala Met Gly
 290 295 300
 Met Gly Asp Ala Phe Ser Glu His Lys Ala Asp Tyr Ser Gly Met Ser
 305 310 315 320
 Ser Gly Ser Gly Leu Tyr Ala Gln Lys Phe Leu His Ser Ser Phe Val
 325 330 335
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 Phe Thr Val Thr Ser Ala Pro Gly His Glu Asn Val His Cys Asn His
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<211> 400

<212> PRT

<213> Homo sapien

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<212> DNA

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<212> PRT

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8948

<210> 120
 <211> 587
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1) ... (587)
 <223> n = A,T,C or G

<400> 120
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 gggctgtgca ntccggtcag ggcgggaagg gaaatgcacc gctgcatgtg aacttacagc 180
 ccaggcggat gccccttccc ttagcactac ctggcctcct gcacccctc gcctcatgtt 240
 cctcccacct tcaanaaatg aanaacccca tgggccacgc cccttgccct ggggaaccaa 300
 ggcagccttc caaaactcag gggctgaagc anactattag ggcaggggct gactttgggt 360
 gacactgccc attcctctc agggcagctc angtcacccn ggnctcttga acccagcctg 420
 ttcttttgaa aaagggcaaa actgaaaagg gcttttctta naaaaagaaa aaccagggaa 480
 ctttgccagg gcttcnntnt taccaaaaacn ncttctcnng gatttttaat tccccattng 540
 gcctccactt accnggggcn atgccccaaa attaanaatt tcccatc 587

<210> 121
 <211> 619
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1) ... (619)
 <223> n = A,T,C or G

<400> 121
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 tgcataaagc caatgtagtc cagtttctaa gatcatgttc caagctaact gaatccact 180
 tcaatacaca ctcatgaact cctgatggaa caataacagg cccaagcctg tggtatgatg 240
 tgcacacttg ctgactcan aaaaaatact actctcataa atgggtggga gtattttgggt 300
 gacaacctac tttgcttggc tgagtgaagg aatgatattc atatattcat ttattccatg 360
 gacatttagt tagtgctttt tatataccag gcatgatgct gagtgacact cttgtgtata 420
 tttccaaatt tttgtacagt cgctgcacat atttgaaatc atatattaag acttccaaaa 480
 aatgaagtcc ctggtttttc atggcaactt gatcagtaaa ggattcnct ctggttggtg 540
 cttaaaacat ctactatatn gttnanatga aattcctttt ccccnctcc cgaaaaaana 600
 aagtgggtgg gaaaaaaa 619

<210> 122
 <211> 1475
 <212> DNA
 <213> Homo sapien

<400> 122
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caaagaaatt	cggagggcag	cactgtgaaa	tagataagtc	aaaaacctgc	tatgagggga	300
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ggaactctgc	cactgtcctt	cagcaaactg	accatgcccc	cagatctgat	gctcttcagc	420
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cggccatcta	caggaggcac	cgggggggct	ctgtcaccta	cgtgtgtgga	ggcagcctca	720
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<210> 123

<211> 2294

<212> DNA

<213> Homo sapien

<400> 123

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tgtgtgtcca	acaagtactt	ctccaacatt	cactggtgca	actgccccaa	gaaattcgga	240
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ggatgtgccc	tgaaggacaa	gccaggcgct	tacagagag	tctcacactt	cttaccctgg	1320
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tatatttcac	tatttttatt	tatatttttg	taatttttaa	taaaagtgat	caataaaatg	2280
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<210> 124

<211> 956

<212> DNA

<213> Homo sapien

<400> 124

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cagattgaga	acctcaagga	ggagctggcc	tacctgaaga	agaaccacga	ggaggagatg	180
aacgccctgc	gaggccaggt	gggtgggtgag	atcaatgtgg	agatggacgc	tgccccaggc	240
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aaccgcaagg	atgccgagga	ttggttcttc	agcaagacag	aggaactgaa	ccgcgaggtg	360
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cgcagcgcgc	ccatctgccc	cacagtctcc	ggcctctcca	gcctcagccc	cctgcttcag	900
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<210> 125

<211> 486

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (486)

<223> n = A,T,C or G

<400> 125

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ttggaaaact	gcttttcttc	tgagaacctt	attctgaatg	tcatcaactt	taccaaacct	180
tctaagtcca	gagctaactt	agtactgttt	aagttactat	tgactgaatt	ttctttcattt	240
tctgttttagc	cagtgttacc	aaggtaagct	ggggaatgaa	gtataccaac	ttctttcaga	300
gcatttttagg	acattatggc	agcttttagaa	ggctgtcttg	tttctagcca	agggagagcc	360

agcgcaggtt	ttggatacta	gagaaagtca	tttgcttgta	ctattgccat	tttagaaagc	420
tctgatgtga	attcaaattt	tacctctgtt	acttaaagcc	aacaatttta	aggcagtagt	480
tttact						486

<210> 126

<211> 3552

<212> DNA

<213> Homo sapien

<400> 126

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<210> 127

<211> 754

<212> DNA

<213> Homo sapien

<400> 127

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accaccttct	aatactttta	atacccaatc	aaaatttatt	atacatatgt	atcatagata	660
ctcatctgta	aagctgtgct	tcaaaatagt	gatctcttcc	caacattaca	atatatatta	720
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<210> 128

<211> 374

<212> DNA

<213> Homo sapien

<400> 128

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ttcccctgcc	cttggttaagt	aactcttgat	ggagaaagga	ttaaagactc	ttatttaacc	180
aaaaaacaga	gccagcta	catttccaaa	ggtagtatc	tcctgtctga	cctcttcttt	240
ggtttaattg	aataaaacta	tatgttcata	tatgtattaa	aacaactcag	aataacatct	300
tttcttctt	agttaaggca	ttataagggc	tatactatca	tccataataa	ccaaggcaat	360
aacttaaaaa	gctg					374

<210> 129

<211> 546

<212> DNA

<213> Homo sapien

<400> 129

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cctcatttct	gcctactgat	ttccttggag	cattcatctg	aatattaccg	tttgctgtgt	180
aacctggtac	atacatagca	tgactccctg	gaatagagtg	ggctgggggtg	cttatgctgg	240
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<210> 130

<211> 5156

<212> DNA

<213> Homo sapien

<400> 130

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<211> 671

<212> DNA

<213> Homo sapien

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 <211> 581
 <212> DNA
 <213> Homo sapien

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 <212> DNA
 <213> Homo sapien

<220>
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<223> n = A,T,C or G

<400> 134

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ctggtccgtg	ggacggtncc	caagccagag	gtgggttcac	ttgtgtaacg	acaataaacg	4740
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<210> 135

<211> 2856

<212> DNA

<213> Homo sapien

<400> 135

tagtcgcggg	tccccgagtg	agcacgccag	ggagcaggag	accaaaccgac	gggggtcgga	60
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cgcacgcccg	tcgccaccgc	cgtaccgggc	gcagccagag	ccaccagcgc	agcgtgcca	180
tggagcccag	cagcaagaag	ctgacgggtc	gcctcatgct	ggctgtggga	ggagcagtgc	240
ttggctccct	gcagtttggc	tacaacactg	gagtcataca	tgccccccag	aagggtgatcg	300
aggagtctta	caaccagaca	tgggtccacc	gctatgggga	gagcatcctg	cccaccacgc	360
tcaccacgct	ctggtccctc	tcagtggcca	tcttttctgt	tgggggcatg	attggctcct	420
tctctgtggg	ccttttcgtt	aacgcctttg	gcccggcgaa	ttcaatgctg	atgatgaacc	480
tgctggcctt	cgtgtccgcc	gtgctcatgg	gcttctcgaa	actgggcaag	tcctttgaga	540
tgctgatcct	gggcccgttc	atcatcggtg	tgtactgcgg	cctgaccaca	ggcttctgtc	600
ccatgtatgt	gggtgaagtg	tcaccacacg	cctttcgtgg	ggccctgggc	accctgcacc	660
agctgggcat	cgtcgtcggc	atcctcatcg	cccagggtgt	cggcctggac	tccatcatgg	720
gcaacaagga	cctgtggccc	ctgctgctga	gcatacatct	catcccggcc	ctgctgcagt	780
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agaaccgggc	caagagtgtg	ctaaagaagc	tgcgcgggac	agctgacgtg	acccatgacc	900
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cccagcagct	gtctggcatc	aacgctgtct	tctattactc	cacgagcatc	ttcgagaagg	1080
cgggggtgca	gcagcctgtg	tatgccacca	ttggctccgg	tatcgtcaac	acggccttca	1140

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aaatctattc	agacaagcaa	cagggtttat	aattttttta	ttactgattt	tgttattttt	1920
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gaggggtggag	actaagccct	gtcgagacac	ttgccttctt	caccagccta	atctgtaggg	2040
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gaggtggcta	tggccacccg	ttctgctggc	ctggatctcc	ccactctagg	ggtcaggctc	2160
cattaggatt	tgccccttcc	catctcttcc	tacccaacca	ctcaaattaa	tctttcttta	2220
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tgcaagatat	ttatatatat	ttttggttgt	caatattaaa	tacagacact	aagttatagt	2460
atatctggac	aagccaactt	gtaaatacac	cacctcactc	ctgttactta	cctaaacaga	2520
tataaatggc	tggtttttag	aaacatggtt	ttgaaatgct	tgtggattga	gggtaggagg	2580
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tttgatccct	gttaccacaga	gaatatatac	attctttatc	ttgacattca	aggcatttct	2760
atcacatatt	tgatagttag	tgttcaaaaa	aacactagtt	ttgtgccagc	cgtgatgctc	2820
aggcttgaaa	tcgcattatt	ttgaatgtga	agggaa			2856

<210> 136

<211> 356

<212> DNA

<213> Homo sapien

<400> 136

gggtggagcca	aatgaagaaa	atgaagatga	aagagacaga	cacctcagtt	tttctggatc	60
aggcattgat	gatgatgaag	attttatctc	cagcaccatt	tcaaccacac	cacgggcttt	120
tgaccacaca	aaacagaacc	aggactggac	tcagtggaac	ccaagccatt	caaatccgga	180
agtgtacttt	cagacaacca	caaggatgac	tgatgtagac	agaaatggca	ccactgctta	240
tgaaggaaac	tggaaaccag	aagcacaccc	tcccctcatt	caccatgagc	atcatgagga	300
agaagagacc	ccacattcta	caagcacaat	ccaggcaact	cctagtagta	caacgg	356

<210> 137

<211> 356

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (356)

<223> n = A,T,C or G

<400> 137

gcaggtggag	aagacatttt	attgttcctg	gggtctctgg	aggccattg	gtggggctgg	60
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gtcactggct	gcccccgaa	cagggcgctg	ctccatggct	ctgcttggtg	tagtctgtgg	120
ctatgtctcc	cagcaaggac	agaaactcag	aaaaatcaat	cttcttatcc	tcattcttgt	180
cctttttctc	aaagacatcg	gcgaggtaat	ttgtgccctt	tttacctcgg	cccgcgacca	240
cgctaaggcc	aaanttcag	acanayggcc	gggcccgtnc	nataggggan	ccaacttgg	300
ggacccaaac	tctggcgcg	aaacacangg	gcataagctt	gnttcctgtg	gggaaa	356

<210> 138

<211> 353

<212> DNA

<213> Homo sapien

<400> 138

aggtccagtc	ctccacttgg	cctgatgaga	gtggggagtg	gcaagggacg	tttctcctgc	60
aatagacact	tagatttctc	tcttggtgga	agaaaccacc	tgtccatcca	ctgactcttc	120
tacattgatg	tggaaattgc	tgtctgctacc	accacctcct	gaagaggctt	ccctgatgcc	180
aatgccagcc	atcttggcat	cctggccctc	gagcaggctg	cggttaagtag	cgatctcctg	240
ctccagcgt	gtctttatgt	caagcagcat	cttgtaactcc	tggttctgag	cctccatctc	300
gcatcggagc	tcactcagac	ctcgscgsg	mssmcgtam	gccgaattcc	agc	353

<210> 139

<211> 371

<212> DNA

<213> Homo sapien

<400> 139

agcgtggctg	cggccgaggt	ccatccgaag	caagattgca	gatggcagtg	tgaagagaga	60
agacatattc	tacacttcaa	agctttggtg	caattcccat	cgaccagagt	tggtccgacc	120
agccttgga	aggtcactga	aaaatcttca	attggattat	gttgacctct	accttattca	180
ttttccagtg	tctgtaaagc	caggtgagga	agtgatccca	aaagatgaaa	atggaaaaat	240
actatttgac	acagtggatc	tctgtgccac	gtgggaggcc	gtggagaagt	gtaaagatgc	300
aggattggac	ctgcccgggc	ggccgctcga	aagccgaatt	ccagcacact	ggcgccggtt	360
actagtggat	c					371

<210> 140

<211> 370

<212> DNA

<213> Homo sapien

<400> 140

tagcgtggtc	gcggccgagg	tccatctccc	tttgggaact	agggggctgc	tggtgggaaa	60
tgggagccag	ggcagatgtt	gcattccctt	gtgtccctgt	aaatgtggga	ctacaagaag	120
aggagctgcc	tgagtgttac	tttctcttcc	tggtaatcct	ctggcccagc	ctcatggcag	180
aatagaggta	tttttaggct	atttttgtaa	tatggcttct	gggtcaaaatc	cctgtgtagc	240
tgaattccca	agccctgcat	tgtacagccc	cccactcccc	tcaccaccta	ataaaggaat	300
agttaacact	caaaaaaaaa	aaaaaacctg	cccgggcggc	cgctcgaaag	ccgaattcca	360
gcacactggc						370

<210> 141

<211> 371

<212> DNA

<213> Homo sapien

<400> 141

tagcgtggtc	gcggccgagg	tcctctgtgc	tgccctgtcac	agcccgatgg	taccagcgca	60
gggtgtaggc	agtgcaggag	ccctcatcca	gtggcaggga	acaggggtca	tcactatccc	120

aaggagcttc agggtcctgg tactcctcca	cagaatactc ggagtattca gagtactcat	180
catcctcagg gggtagccgc tcttctctct	ctgcatgaga gacgcggagc acaggcacag	240
catggagctg ggagccggca gtgtctgcag	cataactagg gaggggtcgt gatccagatg	300
cgatgaactg gccctggcag gcacagtgt	gactcatctc ttggcgacct gcccgggcgg	360
ccgctcgaag c		371

<210> 142

<211> 343

<212> DNA

<213> Homo sapien

<400> 142

gcgttttgag gccaatggtg taaaaggaaa	tatcttcaca taaaaactag atggaagcat	60
tgtcagaaac ctctttgtga tgtttgcttt	caactcacag agttgaacat tccttttcat	120
agagcagttt tgaacactc tttttagaa	tttgcaagcg gatgattgga tcgctatgag	180
gtcttcattg gaaacgggat acctttacat	aaaaactaga cagtagcatt ctcagaaatt	240
tctttgggat gtgggcattc aaccacaga	ggagaacttc atttgataga gcagttttga	300
aacacccttt ttgtagaatc tacaggtgga	catttagagt gct	343

<210> 143

<211> 354

<212> DNA

<213> Homo sapien

<400> 143

aggtctgatg gcagaaaaac tcagactgtc	tgcaacttta cagatggtgc attggttcag	60
catcaggagt gggatgggaa ggaaagcaca	ataacaagaa aattgaaaga tgggaaatta	120
gtggtggagt gtgtcatgaa caatgtcacc	tgtactcgga tctatgaaaa agtagaataa	180
aaattccatc atcacttttg acaggagtta	attaagagaa tgaccaagct cagttcaatg	240
agcaaactc cactactgtt ctttcttttt	tttttcatta ctgtgttcaa ttatctttat	300
cataaacatt ttacatgcag ctatttcaaa	gtgtgttgga ttaattagga tcat	354

<210> 144

<211> 353

<212> DNA

<213> Homo sapien

<400> 144

ggtcaaggac ctgggggacc ccaggtcca	gcagccacat gattctgcag cagacaggga	60
cctagagcac atctggatct cagccccacc	cctggcaacc tgcttgcta gagaactccc	120
aagatgacag actaagtagg attctgccat	ttagaataat tctggtatcc tggcggtgc	180
gttaagtgtc ttaactttca ttctgtctta	cgatagtctt cagaggtggg aacagatgaa	240
gaaaccatgc cccagagaag gttaagtgc	ttcctcttta tggagccagt gttccaacct	300
aggtttgcct gataccagac ctgtggcccc	acctcccatg caggtctctg tgg	353

<210> 145

<211> 371

<212> DNA

<213> Homo sapien

<400> 145

caggtctgtc ataaaactggt ctggagtctc	tgaagactcc ttgttcacca aatgcacat	60
ttcctgagac ttgtggcct ctccgttgag	tccacttggc tttctgtcct ccacagctcc	120
attgccactg ttgatcacta gctttttctt	ctgccacac cttcttcgac tgttgactgc	180
aatgcaaact gcaagaatca aagccaaggc	caagagggat gccaaagatga tcagccattc	240

tggaatttgg ggtgtcctta taggaccaga ggttgtgttt gctccacett cttgactccc	300
atgtgagacc tcggccgga ccacgctaag ccgaattcca gcacactggc ggcccggttac	360
tagtgatcc g	371

<210> 146

<211> 355

<212> DNA

<213> Homo sapien

<400> 146

ggctctccgt cctcttccca gaggtgtcgg ggcttggccc cagcctccat cttcgtctct	60
caggatggcg agtagcagcg gctccaaggc tgaattcatt gtcggaggga aatataaact	120
ggtacggaag atcgggtctg gctccttcgg ggacatctat ttggcgatca acatcaccaa	180
cggcgaggaa gtggcagtga agctagaatc tcagaaggcc aggcaccccc agttgctgta	240
cgagagcaag ctctataaga ttcttcaagg tgggggttggc atccccaca tacggtggta	300
tggtcaggaa aaagactaca atgtactagt catggatctt ctgggaccta gctc	355

<210> 147

<211> 355

<212> DNA

<213> Homo sapien

<400> 147

ggtctgttac aaaatgaaga cagacaacac aacatttact ctgtggagat atcctactca	60
tactatgcac gtgctgtgat tttgaacata actcgtccca aaaacttgtc acgatcatcc	120
tgacttttta ggttggctga tccatcaatc ttgcactcaa ctgttacttc tttcccagtg	180
ttgttaggag caaagctgac ctgaacagca accaatggct gtagataccc aacatgcagt	240
tttttcccat aatatgggaa atattttaag tctatcattc cattatgagg ataaactgct	300
acatttggtat tatcttcatt ctttgaacaa caatctatcc ttggcactcc ttcag	355

<210> 148

<211> 369

<212> DNA

<213> Homo sapien

<400> 148

aggtctctct cccctctctc ctctcctgcc agccaagtga agacatgctt acttcccctt	60
caccttcctt catgatgtgg gaagagtgtc gcaaccagc cctagccaac accgcatgag	120
agggagtgtg ccgagggtt ctgagaaggt ttctctcaca tctagaaaga agcgcttaag	180
atgtggcagc ccctcttctt caagtggctc ttgtcctgtt gcctggggag ttctcaaatt	240
gctgcagcag cctccatcca gcctgaggat gacatcaata cacagaggaa gaagagtcag	300
gaaaagatga gagaagttac agactctcct gggcgacccc gagagcttac cattcctcag	360
acttcttca	369

<210> 149

<211> 620

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(620)

<223> n = A,T,C or G

<400> 149

actagtcaaa	aatgctaaaa	taatttgga	gaaaatattt	tttaagtagt	gttatagttt	60
catgtttatc	ttttattatg	ttttgtgaag	ttgtgtcttt	tcactaatta	cctatactat	120
gccaatattt	ccttatatct	atccataaca	tttatactac	atttgaana	naatatgcac	180
gtgaaactta	acactttata	aggtaaaaat	gaggtttcca	anatttaata	atctgatcaa	240
gttcttggtta	tttccaaata	gaatggactt	ggtctgttaa	gggctaagga	gaagaggaag	300
ataagggttaa	aagtgtgtaa	tgaccaaaaca	ttctaaaaga	aatgcaaaaa	aaaagtttat	360
tttcaagcct	tcgaactatt	taaggaaaagc	aaaatcattt	cctaaatgca	tatcatttgt	420
gagaatttct	cattaatatc	ctgaatcatt	catttccacta	aggctcatgt	tnactccgat	480
atgtctctaa	gaaagtacta	tttcatggtc	caaacctggg	tgccatantt	gggtaaaggc	540
tttcccttaa	gtgtgaaant	attttaaagt	aaattttcct	ctttttaaaa	attccttana	600
aggggttaag	gtgttgggga					620

<210> 150

<211> 371

<212> DNA

<213> Homo sapien

<400> 150

ggtcogatca	aaacctgcta	cctccccaag	actttactag	tgccgataaa	ctttctcaaa	60
gagcaaccag	tatcacttcc	ctgtttataa	aacctctaac	catctctttg	ttctttgaac	120
atgctgaaaa	ccacctggtc	tgcatgtatg	ccogaatttg	yaattctttt	ctctcaaatg	180
aaaatttaat	tttagggatt	catttctata	ttttcacata	tgtagtatta	ttatttcctt	240
atatgtgtaa	ggtgaaattt	atgggtattt	agtgtgcaag	aaaatatatt	tttaaagctt	300
tcatttttcc	cccagtgaat	gatttagaat	tttttatgta	aatatacaga	atgttttttc	360
ttacttttat	a					371

<210> 151

<211> 4655

<212> DNA

<213> Homo sapien

<400> 151

gggacttgag	ttctgttatt	ttcttaagta	gattcatatt	gtaagggtct	cggggtgggg	60
gggttgga	aatcctggag	ccagaagaaa	ggacagcagc	attgatcaat	cttacagcta	120
acatgttgta	cctggaaaac	aatgccaga	ctcaatttag	tgagccacag	tacacgaacc	180
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ataacacaga	ccacgcgcag	aacagcgta	cggcgccctc	gccctacgca	cagcccagct	300
ccaccttcga	tgctctctct	ccatcacccg	ccatccctc	caacaccgac	taccaggcc	360
cgcacagttt	cgacgtgtcc	ttccagcagt	cgagcacccg	caagtcggcc	acctggacgt	420
attccactga	actgaagaaa	ctctactgcc	aaattgcaaa	gacatgcccc	atccagatca	480
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gagggatgaa	ccgccgtcca	attttaatca	tgttactct	ggaaaccaga	gatgggcaag	840
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cggatgaaga	tagcatcaga	aagcagcaag	tttcggacag	tacaaagaac	ggtgatggta	960
cgaagcgc	gtttcgtcag	aacacacatg	gtatccagat	gacatccatc	aagaaacgaa	1020
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tggatgaagat	caaagagtcc	ctggaactca	tgcatgacct	tcttcagcac	acaattgaaa	1140
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agtctccatc	ttcatatggg	aacagctccc	cacctctgaa	caaaatgaac	agcatgaaca	1260
agctgccttc	tgtgagccag	cttatcaacc	ctcagcagcg	caacgcctc	actcctacaa	1320
ccattcctga	tggcatggga	gccaacattc	ccatgatggg	cacccacatg	ccaatggctg	1380

gagacatgaa	tggactcagc	cccacccagg	cactccctcc	cccactctcc	atgccatcca	1440
cctcccactg	cacaccccca	cctccgtatc	ccacagattg	cagcattgtc	agtttcttag	1500
cgagggttggg	ctgttcatca	tgtctggact	atttcacgac	ccaggggctg	accaccatct	1560
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gacatgcgat	ctggaagggc	atcctggacc	accggcagct	ccacgaattc	tcctccccctt	1680
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cccagatga	gtggaatgac	ttcaactttg	acatggatgc	tcgcccgaat	aagcaacagc	1860
gcatacaaga	ggagggggag	tgagcctcac	catgtgagct	cttcctatcc	ctctcctaac	1920
tgccagcccc	ctaaaagcac	tcctgcttaa	tcctcaaaagc	cttctcccta	gctcctcccc	1980
ttcctcttgt	ctgatttctt	aggggaagga	gaagtaagag	gcttacttct	taccctaacc	2040
atctgacctg	gcatactaatt	ctgattctgg	ctttaagcct	tcaaaactat	agcttgcaga	2100
actgtagctt	gccatggcta	ggtagaagtg	agcaaaaaag	agttgggtgt	ctccttaagc	2160
tgcagagatt	tctcattgac	ttttataaag	catgttcacc	cttatagtct	aagactatat	2220
atataaatgt	ataaatatac	agtatagatt	tttgggtggg	gggcattgag	tattgtttaa	2280
aatgtaat	aaatgaaaga	aaattgagtt	gcacttattg	accatttttt	aatttacttg	2340
ttttggatgg	cttgtctata	ctccttcctt	taaggggtat	catgtatgg	gataggtatc	2400
tagagcttaa	tgctacatgt	gagtgcagat	gatgtacaga	ttctttcagt	tccttggatt	2460
ctaaatacat	gccacatcaa	acctttgagt	agatccattt	ccattgctta	ttatgtagg	2520
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<210> 152
 <211> 586
 <212> PRT
 <213> Homo sapien

<400> 152

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		20						25					30		
Gly	Ser	Ser	Ser	Thr	Ser	Pro	Tyr	Asn	Thr	Asp	His	Ala	Gln	Asn	Ser
		35					40					45			
Val	Thr	Ala	Pro	Ser	Pro	Tyr	Ala	Gln	Pro	Ser	Ser	Thr	Phe	Asp	Ala
	50					55					60				
Leu	Ser	Pro	Ser	Pro	Ala	Ile	Pro	Ser	Asn	Thr	Asp	Tyr	Pro	Gly	Pro
65				70						75				80	
His	Ser	Phe	Asp	Val	Ser	Phe	Gln	Gln	Ser	Ser	Thr	Ala	Lys	Ser	Ala
			85						90					95	
Thr	Trp	Thr	Tyr	Ser	Thr	Glu	Leu	Lys	Lys	Leu	Tyr	Cys	Gln	Ile	Ala
			100					105					110		
Lys	Thr	Cys	Pro	Ile	Gln	Ile	Lys	Val	Met	Thr	Pro	Pro	Pro	Gln	Gly
		115					120					125			
Ala	Val	Ile	Arg	Ala	Met	Pro	Val	Tyr	Lys	Lys	Ala	Glu	His	Val	Thr
	130					135					140				
Glu	Val	Val	Lys	Arg	Cys	Pro	Asn	His	Glu	Leu	Ser	Arg	Glu	Phe	Asn
145					150					155				160	
Glu	Gly	Gln	Ile	Ala	Pro	Ser	Ser	His	Leu	Ile	Arg	Val	Glu	Gly	Asn
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Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro	Ile	Thr	Gly	Arg	Gln	Ser	Val
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Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val	Gly	Thr	Glu	Phe	Thr	Thr	Val
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210					215					220					
Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu	Glu	Thr	Arg	Asp	Gly	Gln	Val
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Asp	Arg	Lys	Ala	Asp	Glu	Asp	Ser	Ile	Arg	Lys	Gln	Gln	Val	Ser	Asp
		260					265						270		
Ser	Thr	Lys	Asn	Gly	Asp	Gly	Thr	Lys	Arg	Pro	Phe	Arg	Gln	Asn	Thr
	275					280						285			
His	Gly	Ile	Gln	Met	Thr	Ser	Ile	Lys	Lys	Arg	Arg	Ser	Pro	Asp	Asp
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Glu	Leu	Val	Tyr	Leu	Pro	Val	Arg	Gly	Arg	Glu	Thr	Tyr	Glu	Met	Leu
305				310						315				320	
Val	Lys	Ile	Lys	Glu	Ser	Leu	Glu	Leu	Met	Gln	Tyr	Leu	Leu	Gln	His
			325					330					335		
Thr	Ile	Glu	Thr	Tyr	Arg	Gln	Gln	Gln	Gln	Gln	Gln	His	Gln	His	Leu
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Leu	Gln	Lys	Gln	Thr	Ser	Ile	Gln	Ser	Pro	Ser	Ser	Tyr	Gly	Asn	Ser
		355				360						365			
Ser	Pro	Pro	Leu	Asn	Lys	Met	Asn	Ser	Met	Asn	Lys	Leu	Pro	Ser	Val
370						375						380			

Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr
 385 390 395 400
 Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met
 405 410 415
 Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro
 420 425 430
 Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro
 435 440 445
 Tyr Pro Thr Asp Cys Ser Ile Val Ser Phe Leu Ala Arg Leu Gly Cys
 450 455 460
 Ser Ser Cys Leu Asp Tyr Phe Thr Thr Gln Gly Leu Thr Thr Ile Tyr
 465 470 475 480
 Gln Ile Glu His Tyr Ser Met Asp Asp Leu Ala Ser Leu Lys Ile Pro
 485 490 495
 Glu Gln Phe Arg His Ala Ile Trp Lys Gly Ile Leu Asp His Arg Gln
 500 505 510
 Leu His Glu Phe Ser Ser Pro Ser His Leu Leu Arg Thr Pro Ser Ser
 515 520 525
 Ala Ser Thr Val Ser Val Gly Ser Ser Glu Thr Arg Gly Glu Arg Val
 530 535 540
 Ile Asp Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro
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 Arg Asp Glu Trp Asn Asp Phe Asn Phe Asp Met Asp Ala Arg Arg Asn
 565 570 575
 Lys Gln Gln Arg Ile Lys Glu Glu Gly Glu
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<210> 153
 <211> 2007
 <212> DNA
 <213> Homo sapien

<400> 153

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cttgaccaaa	tgccctggag	ctccagcgcc	ttggagctga	ggtgggtcaa	ggtgacctga	240
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<210> 154

<211> 2148

<212> DNA

<213> Homo sapien

<400> 154

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<210> 155
 <211> 153
 <212> PRT
 <213> Homo sapien

<400> 155
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 35 40 45
 Ala Ala Val Ser Ser Ile Phe Asn Ser Pro Glu Glu Phe Leu Gly Lys
 50 55 60
 Ala Val Gly Leu Ser Ala Glu Ala Leu Thr Ile Gln Gln Tyr Ala Asp
 65 70 75 80
 Val Leu Ser Lys Ala Leu Gly Lys Glu Val Arg Asp Ala Lys Ile Thr
 85 90 95
 Pro Glu Ala Phe Glu Lys Leu Gly Phe Pro Ala Ala Lys Glu Ile Ala
 100 105 110
 Asn Met Cys Arg Phe Tyr Glu Met Lys Pro Asp Arg Asp Val Asn Leu
 115 120 125
 Thr His Gln Leu Asn Pro Lys Val Lys Ser Phe Ser Gln Phe Ile Ser
 130 135 140
 Glu Asn Gln Gly Ala Phe Lys Gly Met
 145 150

<210> 156
 <211> 128
 <212> PRT
 <213> Homo sapien

<400> 156
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 Trp Arg Pro Val Lys Ala Ser Asp Gly Asp Tyr Tyr Thr Leu Ala Val
 20 25 30
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 35 40 45
 Ala Ala Val Ser Ser Ile Phe Asn Ser Pro Glu Glu Phe Leu Gly Lys
 50 55 60
 Ala Val Gly Leu Ser Ala Glu Ala Leu Thr Ile Gln Gln Tyr Ala Asp
 65 70 75 80
 Val Leu Ser Lys Ala Leu Gly Lys Glu Val Arg Asp Ala Lys Thr Ile
 85 90 95
 Cys Ala Ile Asp Asp Gln Lys Thr Val Glu Glu Gly Phe Met Glu Asp
 100 105 110
 Val Gly Leu Ser Trp Ser Leu Arg Glu His Asp His Val Ala Gly Ala
 115 120 125

<210> 157
 <211> 424
 <212> DNA
 <213> Homo sapien

<220>
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 <223> n = A,T,C or G

<400> 157

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aattcagtc	ccactgttat	attaccttct	ccaggaaccc	tccagtgggg	aaggctgcga	180
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tgct						424

<210> 158
 <211> 2099
 <212> DNA
 <213> Homo sapien

<400> 158

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cggaacagtg tggaagcaga aggttttttt aactcatccg tttgccaatc attgcaaaca 2040
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<210> 159

<211> 291

<212> PRT

<213> Homo sapien

<400> 159

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Val Met Ile Leu Val Val Ala Ala Gln Glu Val Trp Gly Asp Glu Gln
35 40 45
Glu Asp Phe Val Cys Asn Thr Leu Gln Pro Gly Cys Lys Asn Val Cys
50 55 60
Tyr Asp His Phe Phe Pro Val Ser His Ile Arg Leu Trp Ala Leu Gln
65 70 75 80
Leu Ile Phe Val Ser Thr Pro Ala Leu Leu Val Ala Met His Val Ala
85 90 95
Tyr Tyr Arg His Glu Thr Thr Arg Lys Phe Arg Arg Gly Glu Lys Arg
100 105 110
Asn Asp Phe Lys Asp Ile Glu Asp Ile Lys Lys Gln Lys Val Arg Ile
115 120 125
Glu Gly Ser Leu Trp Trp Thr Tyr Thr Ser Ser Ile Phe Phe Arg Ile
130 135 140
Ile Phe Glu Ala Ala Phe Met Tyr Val Phe Tyr Phe Leu Tyr Asn Gly
145 150 155 160
Tyr His Leu Pro Trp Val Leu Lys Cys Gly Ile Asp Pro Cys Pro Asn
165 170 175
Leu Val Asp Cys Phe Ile Ser Arg Pro Thr Glu Lys Thr Val Phe Thr
180 185 190
Ile Phe Met Ile Ser Ala Ser Val Ile Cys Met Leu Leu Asn Val Ala
195 200 205
Glu Leu Cys Tyr Leu Leu Leu Lys Val Cys Phe Arg Arg Ser Lys Arg
210 215 220
Ala Gln Thr Gln Lys Asn His Pro Asn His Ala Leu Lys Glu Ser Lys
225 230 235 240
Gln Asn Glu Met Asn Glu Leu Ile Ser Asp Ser Gly Gln Asn Ala Ile
245 250 255
Thr Gly Ser Gln Ala Lys His Phe Lys Val Lys Cys Ser Cys Val Ile
260 265 270
Arg Arg Leu Leu Ser Ser Pro Glu Gly Asn Thr Asn Leu Lys Val Pro
275 280 285
Ser Val Ala
290

<210> 160

<211> 3951

<212> DNA

<213> Homo sapien

<400> 160

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<210> 161

<211> 943

<212> PRT

<213> Homo sapien

<400> 161

Met Thr Gln Arg Ser Ile Ala Gly Pro Ile Cys Asn Leu Lys Phe Val	1	5	10	15
Thr Leu Leu Val Ala Leu Ser Ser Glu Leu Pro Phe Leu Gly Ala Gly	20	25	30	
Val Gln Leu Gln Asp Asn Gly Tyr Asn Gly Leu Leu Ile Ala Ile Asn	35	40	45	
Pro Gln Val Pro Glu Asn Gln Asn Leu Ile Ser Asn Ile Lys Glu Met	50	55	60	
Ile Thr Glu Ala Ser Phe Tyr Leu Phe Asn Ala Thr Lys Arg Arg Val	65	70	75	80
Phe Phe Arg Asn Ile Lys Ile Leu Ile Pro Ala Thr Trp Lys Ala Asn	85	90	95	
Asn Asn Ser Lys Ile Lys Gln Glu Ser Tyr Glu Lys Ala Asn Val Ile	100	105	110	
Val Thr Asp Trp Tyr Gly Ala His Gly Asp Asp Pro Tyr Thr Leu Gln	115	120	125	
Tyr Arg Gly Cys Gly Lys Glu Gly Lys Tyr Ile His Phe Thr Pro Asn	130	135	140	
Phe Leu Leu Asn Asp Asn Leu Thr Ala Gly Tyr Gly Ser Arg Gly Arg	145	150	155	160
Val Phe Val His Glu Trp Ala His Leu Arg Trp Gly Val Phe Asp Glu	165	170	175	
Tyr Asn Asn Asp Lys Pro Phe Tyr Ile Asn Gly Gln Asn Gln Ile Lys	180	185	190	
Val Thr Arg Cys Ser Ser Asp Ile Thr Gly Ile Phe Val Cys Glu Lys	195	200	205	
Gly Pro Cys Pro Gln Glu Asn Cys Ile Ile Ser Lys Leu Phe Lys Glu	210	215	220	
Gly Cys Thr Phe Ile Tyr Asn Ser Thr Gln Asn Ala Thr Ala Ser Ile	225	230	235	240
Met Phe Met Gln Ser Leu Ser Ser Val Val Glu Phe Cys Asn Ala Ser	245	250	255	
Thr His Asn Gln Glu Ala Pro Asn Leu Gln Asn Gln Met Cys Ser Leu	260	265	270	
Arg Ser Ala Trp Asp Val Ile Thr Asp Ser Ala Asp Phe His His Ser	275	280	285	
Phe Pro Met Asn Gly Thr Glu Leu Pro Pro Pro Thr Phe Ser Leu	290	295	300	

Val Glu Ala Gly Asp Lys Val Val Cys Leu Val Leu Asp Val Ser Ser
 305 310 315 320
 Lys Met Ala Glu Ala Asp Arg Leu Leu Gln Leu Gln Gln Ala Ala Glu
 325 330 335
 Phe Tyr Leu Met Gln Ile Val Glu Ile His Thr Phe Val Gly Ile Ala
 340 345 350
 Ser Phe Asp Ser Lys Gly Glu Ile Arg Ala Gln Leu His Gln Ile Asn
 355 360 365
 Ser Asn Asp Asp Arg Lys Leu Leu Val Ser Tyr Leu Pro Thr Thr Val
 370 375 380
 Ser Ala Lys Thr Asp Ile Ser Ile Cys Ser Gly Leu Lys Lys Gly Phe
 385 390 395 400
 Glu Val Val Glu Lys Leu Asn Gly Lys Ala Tyr Gly Ser Val Met Ile
 405 410 415
 Leu Val Thr Ser Gly Asp Asp Lys Leu Leu Gly Asn Cys Leu Pro Thr
 420 425 430
 Val Leu Ser Ser Gly Ser Thr Ile His Ser Ile Ala Leu Gly Ser Ser
 435 440 445
 Ala Ala Pro Asn Leu Glu Glu Leu Ser Arg Leu Thr Gly Gly Leu Lys
 450 455 460
 Phe Phe Val Pro Asp Ile Ser Asn Ser Asn Ser Met Ile Asp Ala Phe
 465 470 475 480
 Ser Arg Ile Ser Ser Gly Thr Gly Asp Ile Phe Gln Gln His Ile Gln
 485 490 495
 Leu Glu Ser Thr Gly Glu Asn Val Lys Pro His His Gln Leu Lys Asn
 500 505 510
 Thr Val Thr Val Asp Asn Thr Val Gly Asn Asp Thr Met Phe Leu Val
 515 520 525
 Thr Trp Gln Ala Ser Gly Pro Pro Glu Ile Ile Leu Phe Asp Pro Asp
 530 535 540
 Gly Arg Lys Tyr Tyr Thr Asn Asn Phe Ile Thr Asn Leu Thr Phe Arg
 545 550 555 560
 Thr Ala Ser Leu Trp Ile Pro Gly Thr Ala Lys Pro Gly His Trp Thr
 565 570 575
 Tyr Thr Leu Asn Asn Thr His His Ser Leu Gln Ala Leu Lys Val Thr
 580 585 590
 Val Thr Ser Arg Ala Ser Asn Ser Ala Val Pro Pro Ala Thr Val Glu
 595 600 605
 Ala Phe Val Glu Arg Asp Ser Leu His Phe Pro His Pro Val Met Ile
 610 615 620
 Tyr Ala Asn Val Lys Gln Gly Phe Tyr Pro Ile Leu Asn Ala Thr Val
 625 630 635 640
 Thr Ala Thr Val Glu Pro Glu Thr Gly Asp Pro Val Thr Leu Arg Leu
 645 650 655
 Leu Asp Asp Gly Ala Gly Ala Asp Val Ile Lys Asn Asp Gly Ile Tyr
 660 665 670
 Ser Arg Tyr Phe Phe Ser Phe Ala Asn Gly Arg Tyr Ser Leu Lys
 675 680 685
 Val His Val Asn His Ser Pro Ser Ile Ser Thr Pro Ala His Ser Ile
 690 695 700
 Pro Gly Ser His Ala Met Tyr Val Pro Gly Tyr Thr Ala Asn Gly Asn
 705 710 715 720
 Ile Gln Met Asn Ala Pro Arg Lys Ser Val Gly Arg Asn Glu Glu Glu
 725 730 735
 Arg Lys Trp Gly Phe Ser Arg Val Ser Ser Gly Gly Ser Phe Ser Val

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<210> 162
<211> 498
<212> DNA
<213> Homo sapien
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<400> 162						
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agcccctcaa	gtcgggtatg	aaggagctgg	ccgtgttccg	ggagaaggtc	actgagcagc	120
accggcagat	gggcaagggt	ggcaagcatc	accttggcct	ggaggagccc	aagaagctgc	180
gaccaccccc	tgccaggact	ccctgccaac	aggaaactgga	ccaggtcctg	gagcggatct	240
ccaccatgcg	ccttcgggat	gagcggggcc	ctctggagca	cctctactcc	ctgcacatcc	300
ccaactgtga	caagcatggc	ctgtacaacc	tcaaacagtg	gcaagatgtc	tctgaacggg	360
cagcgtgggg	agtgtcgtg	tgtgaacccc	aacacoggga	agctgatcca	gggagccccc	420
accatccggg	gggaccccg	gtgtcatctc	ttctacaatg	agcagcagga	ggctcgcggg	480
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<210> 163
<211> 1128
<212> DNA
<213> Homo sapien
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<400> 163						
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cctcctgcg	gcgctcggtg	gaggggtctca	gcgcgcgcct	caaaagagct	gtgtctgaac	240
atcagctcct	ccatgacaa	gggaagtcca	tccaagattt	acgcgcacga	ttcttccctc	300
accatctgat	cgcacaatac	cacacagctg	aaatcgagac	tacctcgagc	gtgtcccta	360
actccaagcc	ctctcccaac	acaaagaacc	accccgtcgc	atttgggtct	gatgatgaag	420

gcagatacct	aactcaggaa	actaacaagg	tgagagcgta	caaagagcag	ccgctcaaga	480
cacctgggaa	gaaaaagaaa	ggcaagcccg	ggaaacgcaa	ggagcaggaa	aagaaaaaac	540
ggcgaactcg	ctctgcctgg	ttagactctg	gagtgcactg	gagtgggcta	gaaggggacc	600
acctgtctga	cacctccaca	acgtcgctgg	agctcgattc	acggaggcat	tgaatttttc	660
agcagagacc	ttccaaggac	atattgcagg	attctgtaat	agtgaacata	tggaaagtat	720
tagaaaatatt	tattgtctgt	aaatactgta	aatgcattgg	aataaaactg	tctcccccatt	780
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tgtatcttgg	tgctgctgaa	tttctatatt	ttttgtaaca	taatgcactt	tagatataca	960
tatcaagtat	gttgataaat	gacacaatga	agtgtctcta	ttttgtgggt	gatttttaatg	1020
aatgcctaaa	tataattatc	caaattgatt	ttcctttgtg	catgtaaaaa	taacagtatt	1080
ttaaatttgt	aaagaatgtc	taataaaata	taatctaatt	acatcatg		1128

<210> 164

<211> 1310

<212> DNA

<213> Homo sapien

<400> 164

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gagacgtgta	aacacactac	ttatcattga	tgcatatata	aaaccatttt	attttcgcta	180
ttatttcaga	ggaagcgctt	ctgatttgtt	tcttttttcc	ctttttgtct	tttctggctg	240
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cgcggtgccc	tcctgcgggc	gctcgttgga	gggtctcagc	cgccgcctca	aaagagctgt	420
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gtcccctaac	tccaagccct	ctcccaacac	aaagaaccac	cccgtccgat	ttgggtctga	600
tgatgagggc	agatacctaa	ctcaggaaac	taacaagggtg	gagacgtaca	aagagcagcc	660
gctcaagaca	cctggaaga	aaaagaaagg	caagccggg	aaacgcaagg	agcaggaaaa	720
gaaaaaacgg	cgaactcgct	ctgcctgggt	agactctgga	gtgactggga	gtgggctaga	780
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aaattttcag	cagagacctt	ccaaggacat	attgcaggat	tctgtaatag	tgaacatatg	900
gaaagtatta	gaaatattta	ttgtctgtaa	atactgtaaa	tgcatgggaa	taaaactgtc	960
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ttttaatgaa	tgctaaata	taattatcca	aattgatttt	cctttgtgcc	cgtaaaaata	1260
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<210> 165

<211> 177

<212> PRT

<213> Homo sapien

<400> 165

Met	Gln	Arg	Arg	Leu	Val	Gln	Gln	Trp	Ser	Val	Ala	Val	Phe	Leu	Leu
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Ser	Tyr	Ala	Val	Pro	Ser	Cys	Gly	Arg	Ser	Val	Glu	Gly	Leu	Ser	Arg
			20				25				30				
Arg	Leu	Lys	Arg	Ala	Val	Ser	Glu	His	Gln	Leu	Leu	His	Asp	Lys	Gly
		35				40				45					
Lys	Ser	Ile	Gln	Asp	Leu	Arg	Arg	Arg	Phe	Phe	Leu	His	His	Leu	Ile

50		55		60
Ala Glu Ile His Thr	Ala Glu Ile Arg	Ala Thr Ser Glu Val Ser Pro		
65	70	75		80
Asn Ser Lys Pro Ser Pro	Asn Thr Lys Asn His Pro Val Arg Phe Gly			
	85	90		95
Ser Asp Asp Glu Gly Arg Tyr Leu Thr	Gln Glu Thr Asn Lys Val Glu			
	100	105		110
Thr Tyr Lys Glu Gln Pro Leu Lys Thr	Pro Gly Lys Lys Lys Lys Gly			
	115	120		125
Lys Pro Gly Lys Arg Lys Glu Gln Glu Lys Lys Lys Arg Arg Thr Arg				
	130	135		140
Ser Ala Trp Leu Asp Ser Gly Val Thr Gly Ser Gly Leu Glu Gly Asp				
145	150	155		160
His Leu Ser Asp Thr Ser Thr Thr Ser Leu Glu Leu Asp Ser Arg Arg				
	165	170		175

His

<210> 166
 <211> 177
 <212> PRT
 <213> Homo sapien

<400> 166
Met Gln Arg Arg Leu Val Gln Gln Trp Ser Val Ala Val Phe Leu Leu
1 5 10 15
Ser Tyr Ala Val Pro Ser Cys Gly Arg Ser Val Glu Gly Leu Ser Arg
20 25 30
Arg Leu Lys Arg Ala Val Ser Glu His Gln Leu Leu His Asp Lys Gly
35 40 45
Lys Ser Ile Gln Asp Leu Arg Arg Arg Phe Phe Leu His His Leu Ile
50 55 60
Ala Glu Ile His Thr Ala Glu Ile Arg Ala Thr Ser Glu Val Ser Pro
65 70 75 80
Asn Ser Lys Pro Ser Pro Asn Thr Lys Asn His Pro Val Arg Phe Gly
85 90 95
Ser Asp Asp Glu Gly Arg Tyr Leu Thr Gln Glu Thr Asn Lys Val Glu
100 105 110
Thr Tyr Lys Glu Gln Pro Leu Lys Thr Pro Gly Lys Lys Lys Gly
115 120 125
Lys Pro Gly Lys Arg Lys Glu Gln Glu Lys Lys Lys Arg Arg Thr Arg
130 135 140
Ser Ala Trp Leu Asp Ser Gly Val Thr Gly Ser Gly Leu Glu Gly Asp
145 150 155 160
His Leu Ser Asp Thr Ser Thr Thr Ser Leu Glu Leu Asp Ser Arg Arg
165 170 175

His

<210> 167
 <211> 3362
 <212> DNA
 <213> Homo sapien

<400> 167

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ttcagaactc	ccattcctgg	gagctggagt	acagcttcaa	gacaatgggt	ataatggatt	180
gctcattgca	attaatcctc	aggtaacctga	gaatcagaac	ctcatctcaa	acattaagga	240
aatgataaact	gaagcttcat	tttacctatt	taatgctacc	aagagaagag	tattttttcag	300
aaatataaag	attttaatac	ctgccacatg	gaaagctaata	aataacagca	aaataaaaca	360
agaatcatat	gaaaaggcaa	atgtcatagt	gactgactgg	tatggggcac	atggagatga	420
tccatacacc	ctacaatata	gaggggtgtg	aaaagaggga	aaatacattc	atttcacacc	480
taatttccta	ctgaatgata	acttaacagc	tggctacgga	tcacgaggcc	gagtgtttgt	540
ccatgaatgg	gcccacctcc	gttgggggtg	gttcgatgag	tataacaatg	acaaaccttt	600
ctacataaat	gggcaaaatc	aaattaaagt	gacaaggtgt	tcactctgaca	tcacaggcat	660
ttttgtgtgt	gaaaaaggct	cttgccccc	agaaaactgt	attattagta	agcttttttaa	720
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<210> 168

<211> 2784

<212> DNA

<213> Homo sapien

<400> 168

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2784

<210> 169

<211> 592

<212> PRT

<213> Homo sapien

<400> 169

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 35 40 45
 Pro Gln Val Pro Glu Asn Gln Asn Leu Ile Ser Asn Ile Lys Glu Met
 50 55 60
 Ile Thr Glu Ala Ser Phe Tyr Leu Phe Asn Ala Thr Lys Arg Arg Val
 65 70 75 80
 Phe Phe Arg Asn Ile Lys Ile Leu Ile Pro Ala Thr Trp Lys Ala Asn
 85 90 95
 Asn Asn Ser Lys Ile Lys Gln Glu Ser Tyr Glu Lys Ala Asn Val Ile
 100 105 110
 Val Thr Asp Trp Tyr Gly Ala His Gly Asp Asp Pro Tyr Thr Leu Gln
 115 120 125
 Tyr Arg Gly Cys Gly Lys Glu Gly Lys Tyr Ile His Phe Thr Pro Asn
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 Phe Leu Leu Asn Asp Asn Leu Thr Ala Gly Tyr Gly Ser Arg Gly Arg
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 Val Phe Val His Glu Trp Ala His Leu Arg Trp Gly Val Phe Asp Glu
 165 170 175
 Tyr Asn Asn Asp Lys Pro Phe Tyr Ile Asn Gly Gln Asn Gln Ile Lys
 180 185 190
 Val Thr Arg Cys Ser Ser Asp Ile Thr Gly Ile Phe Val Cys Glu Lys
 195 200 205
 Gly Pro Cys Pro Gln Glu Asn Cys Ile Ile Ser Lys Leu Phe Lys Glu
 210 215 220
 Gly Cys Thr Phe Ile Tyr Asn Ser Thr Gln Asn Ala Thr Ala Ser Ile
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 Val Glu Ala Gly Asp Lys Val Val Cys Leu Val Leu Asp Val Ser Ser
 305 310 315 320
 Lys Met Ala Glu Ala Asp Arg Leu Leu Gln Leu Gln Gln Ala Ala Glu
 325 330 335
 Phe Tyr Leu Met Gln Ile Val Glu Ile His Thr Phe Val Gly Ile Ala
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 Ser Phe Asp Ser Lys Gly Glu Ile Arg Ala Gln Leu His Gln Ile Asn
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Ala Ala Pro Asn Leu Glu Glu Leu Ser Arg Leu Thr Gly Gly Leu Lys		445
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Phe Phe Val Pro Asp Ile Ser Asn Ser Asn Ser Met Ile Asp Ala Phe		460
465	470	475
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	485	490
Leu Glu Ser Thr Gly Glu Asn Val Lys Pro His His Gln Leu Lys Asn		495
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Thr Val Thr Val Asp Asn Thr Val Gly Asn Asp Thr Met Phe Leu Val		510
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Gly Arg Lys Tyr Tyr Thr Asn Asn Phe Ile Thr Asn Leu Thr Phe Arg		540
545	550	555
Thr Ala Ser Leu Trp Ile Pro Gly Thr Ala Lys Pro Gly His Trp Thr		560
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<210> 170

<211> 791

<212> PRT

<213> Homo sapien

<400> 170

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Pro Gln Val Pro Glu Asn Gln Asn Leu Ile Ser Asn Ile Lys Glu Met	40
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Ile Thr Glu Ala Ser Phe Tyr Leu Phe Asn Ala Thr Lys Arg Arg Val	55
65	70
Phe Phe Arg Asn Ile Lys Ile Leu Ile Pro Ala Thr Trp Lys Ala Asn	75
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Asn Asn Ser Lys Ile Lys Gln Glu Ser Tyr Glu Lys Ala Asn Val Ile	90
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Val Thr Asp Trp Tyr Gly Ala His Gly Asp Asp Pro Tyr Thr Leu Gln	105
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Tyr Arg Gly Cys Gly Lys Glu Gly Lys Tyr Ile His Phe Thr Pro Asn	120
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Phe Leu Leu Asn Asp Asn Leu Thr Ala Gly Tyr Gly Ser Arg Gly Arg	135
145	150
Val Phe Val His Glu Trp Ala His Leu Arg Trp Gly Val Phe Asp Glu	155
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 Leu Asp Asp Gly Ala Gly Ala Asp Val Ile Lys Asn Asp Gly Ile Tyr
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 Ser Arg Tyr Phe Phe Ser Phe Ala Ala Asn Gly Arg Tyr Ser Leu Lys
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 Val His Val Asn His Ser Pro Ser Ile Ser Thr Pro Ala His Ser Ile
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 Ile Gln Met Asn Ala Pro Arg Lys Ser Val Gly Arg Asn Glu Glu Glu
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 Leu Gly Val Pro Ala Gly Pro His Pro Asp Val Phe Pro Pro Cys Lys
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<210> 171

<211> 1491

<212> DNA

<213> Homo sapien

<400> 171

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1491

<210> 172

<211> 364

<212> PRT

<213> Homo sapien

<400> 172

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Ser Gln Glu Gly Gly Gly Ser Gly Ser Tyr Glu Glu Gly Cys Gln Ser		
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<211> 580

<212> PRT

<213> Homo sapiens

<400> 176

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20 25 30

Phe Leu Val Lys Thr Gly Tyr Ala Phe Val Asp Cys Pro Asp Glu Ser
35 40 45

Trp Ala Leu Lys Ala Ile Glu Ala Leu Ser Gly Lys Ile Glu Leu His
50 55 60

Gly Lys Pro Ile Glu Val Glu His Ser Val Pro Lys Arg Gln Arg Ile
65 70 75 80

Arg Lys Leu Gln Ile Arg Asn Ile Pro Pro His Leu Gln Trp Glu Val
85 90 95

Leu Asp Ser Leu Leu Val Gln Tyr Gly Val Val Glu Ser Cys Glu Gln
100 105 110

Val Asn Thr Asp Ser Glu Thr Ala Val Val Asn Val Thr Tyr Ser Ser
115 120 125

Lys Asp Gln Ala Arg Gln Ala Leu Asp Lys Leu Asn Gly Phe Gln Leu
130 135 140

Glu Asn Phe Thr Leu Lys Val Ala Tyr Ile Pro Asp Glu Met Ala Ala
145 150 155 160

Gln Gln Asn Pro Leu Gln Gln Pro Arg Gly Arg Arg Gly Leu Gly Gln
165 170 175

Arg Gly Ser Ser Arg Gln Gly Ser Pro Gly Ser Val Ser Lys Gln Lys
180 185 190

Pro Cys Asp Leu Pro Leu Arg Leu Leu Val Pro Thr Gln Phe Val Gly
195 200 205

Ala Ile Ile Gly Lys Glu Gly Ala Thr Ile Arg Asn Ile Thr Lys Gln
210 215 220

Thr Gln Ser Lys Ile Asp Val His Arg Lys Glu Asn Ala Gly Ala Ala
225 230 235 240

Glu Lys Ser Ile Thr Ile Leu Ser Thr Pro Glu Gly Thr Ser Ala Ala
245 250 255

Cys Lys Ser Ile Leu Glu Ile Met His Lys Glu Ala Gln Asp Ile Lys
 260 265 270
 Phe Thr Glu Glu Ile Pro Leu Lys Ile Leu Ala His Asn Asn Phe Val
 275 280 285
 Gly Arg Leu Ile Gly Lys Glu Gly Arg Asn Leu Lys Lys Ile Glu Gln
 290 295 300
 Asp Thr Asp Thr Lys Ile Thr Ile Ser Pro Leu Gln Glu Leu Thr Leu
 305 310 315 320
 Tyr Asn Pro Glu Arg Thr Ile Thr Val Lys Gly Asn Val Glu Thr Cys
 325 330 335
 Ala Lys Ala Glu Glu Glu Ile Met Lys Lys Ile Arg Glu Ser Tyr Glu
 340 345 350
 Asn Asp Ile Ala Ser Met Asn Leu Gln Ala His Leu Ile Pro Gly Leu
 355 360 365
 Asn Leu Asn Ala Leu Gly Leu Phe Pro Pro Thr Ser Gly Met Pro Pro
 370 375 380
 Pro Thr Ser Gly Pro Pro Ser Ala Met Thr Pro Pro Tyr Pro Gln Phe
 385 390 395 400
 Glu Gln Ser Glu Thr Glu Thr Val His Gln Phe Ile Pro Ala Leu Ser
 405 410 415
 Val Gly Ala Ile Ile Gly Lys Gln Gly Gln His Ile Lys Gln Leu Ser
 420 425 430
 Arg Phe Ala Gly Ala Ser Ile Lys Ile Ala Pro Ala Glu Ala Pro Asp
 435 440 445
 Ala Lys Val Arg Met Val Ile Ile Thr Gly Pro Pro Glu Ala Gln Phe
 450 455 460
 Lys Ala Gln Gly Arg Ile Tyr Gly Lys Ile Lys Glu Glu Asn Phe Val
 465 470 475 480
 Ser Pro Lys Glu Glu Val Lys Leu Glu Ala His Ile Arg Val Pro Ser
 485 490 495
 Phe Ala Ala Gly Arg Val Ile Gly Lys Gly Gly Lys Thr Val Asn Glu
 500 505 510
 Leu Gln Asn Leu Ser Ser Ala Glu Val Val Val Pro Arg Asp Gln Thr
 515 520 525
 Pro Asp Glu Asn Asp Gln Val Val Val Lys Ile Thr Gly His Phe Tyr
 530 535 540

Ala Cys Gln Val Ala Gln Arg Lys Ile Gln Glu Ile Leu Thr Gln Val
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Lys Gln His Gln Gln Gln Lys Ala Leu Gln Ser Gly Pro Pro Gln Ser
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Arg Arg Lys

<210> 177

<211> 401

<212> DNA

<213> Homo sapiens

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 cacacagcaa aaaattgttt actttgttgg acaaaccaaa tcagttctca aaaaatgacc 180
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 gaagtgagct tgtgcttagt atttacattg gatgccagtt ttgtaatcac tgacttatgt 300
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<210> 178

<211> 561

<212> DNA

<213> Homo sapiens

<400> 178

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 gcagccaaag acctaactca gtcccctgag gtctcccca caaccatcca ggtgacatac 240
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<210> 179

<211> 521

<212> DNA

<213> Homo sapiens

<400> 179

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521

<210> 180

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<212> DNA

<213> Homo sapiens

<400> 180

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 tggctttcct cgcgaagcgg atgaacacca acccttcccg agggccctac cacttccggg 240
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 gccaggccgc tctggaccgt ctcaagggtg ttgacggcat cccaccgcc tacgacaaga 360
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<210> 181

<211> 283

<212> DNA

<213> Homo sapiens

<220>

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<222> (35)

<223> n=A,T,C or G

<400> 181

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 caagtagtgt cttctacct atctccagat acatgtcaaa aaa 283

<210> 182

<211> 401

<212> DNA

<213> Homo sapiens

<400> 182

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 agaggattga gtaagtagtt ggatggcttt cataaaaaca agaattcaag aagaggattc 180
 atgctttaag aaacatttgt tataattcc tcacaaatta tacctgggat aaaaactatg 240
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<210> 183

<211> 366

<212> DNA

<213> Homo sapiens

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<221> unsure

<222> (325)

<223> n=A,T,C or G

<400> 183

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aaaaaa 366

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<210> 184

<211> 370

<212> DNA

<213> Homo sapiens

<400> 184

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taaaatgtta gtctacatag atgggtgatt gtaactttat tgccattaaa agatttcaaa 180
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tcagtctgct ctgtttaatt ctgctgtctg ctctctctta atgctgcgtc cctaattgta 300
cacagtttag tgatatctag gagtataaag ttgtcgccca tcaataaaaa tcacaaagtt 360
ggtttaaaaa 370

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<210> 185

<211> 107

<212> DNA

<213> Homo sapiens

<400> 185

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gttggtgttt attttctggt agtcaccttc cccatttaa aaaaaa 107

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<210> 186

<211> 309

<212> DNA

<213> Homo sapiens

<400> 186

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gccagtgagt gacagtcag agggagtgtc tcttcttggg gaggaagaa ggtagagcct 180
ttctgtctga atgaaaggcc aaggctacag tacaggcccc cgccccagcc aggggtgttaa 240
tgcccacgta gtggaggcct ctggcagatc ctgcattcca aggtcactgg actgtacgtt 300
tttatggtt 309

```

<210> 187

<211> 477

<212> DNA

<213> Homo sapiens

<400> 187

```

ttcagtccca gcaagaagcg agaattctga gatcctccag aaagtcgagc agcaccacc 60
tccaacctcg ggccagtgtc ttcaggcttt actggggacc tgcgagctgg cctaattgtg 120

```

```

tggcctgcaa gccaggccat ccctgggcgc cacagacgag ctccgagcca ggtcaggctt 180
cggaggccac aagctcagcc tcaggccdag gcaactgattg tggcagaggg gccactaccc 240
aaggtctagc taggccaag acctagttac ccagacagtg agaagcccct ggaaggcaga 300
aaagtggga gcatggcaga caggggaagg aaacattttc agggaaaaga catgtatcac 360
atgtcttcag aagcaagtca ggtttcatgt aaccgagtgt cctcttgctg gtccaaaagt 420
agcccagggc ttagcacag gttcacagt gattttgtgt tcagccgtga gtcacac 477

```

<210> 188

<211> 220

<212> DNA

<213> Homo sapiens

<400> 188

```

taaatatggg agatattaat attcctctta gatgaccagt gattccaatt gtcccaagtt 60
ttaaataagt accctgtgag tatgagataa attagtgaca atcagaacaa gtttcagtat 120
cagatgttca agaggaagtt gctattgeat tgattttaat attgtacat aaacactgat 180
ttttttgagc attattttgt attgtgtgta ctttaatacc 220

```

<210> 189

<211> 417

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (76)

<223> n=A,T,C or G

<221> unsure

<222> (77)

<223> n=A,T,C or G

<400> 189

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accatcttga cagaggatac atgctcccaa aacgtttgtt accacactta aaaatcactg 60
ccatcattaa gcatcnnttt caaaattata gccattcatg atttactttt tccagatgac 120
tatcattatt ctagtccctt gaatttgtaa ggggaaaaaa aacaaaaaça aaaacttacg 180
atgcaacttt ctccagcaca tcagatttca aattgaaaat taaagacatg ctatggtaat 240
gcacttgcta gtactacaca ctttgtacaa caaaaaacag aggcaagaaa caacggaaag 300
agaaaagcct tcctttgttg gcccttaaac tgagtcaaga tctgaaatgt agagatgatc 360
tctgacgata cctgtatgtt cttattgtgt aaataaaatt gctggtatga aatgaca 417

```

<210> 190

<211> 497

<212> DNA

<213> Homo sapiens

<400> 190

```

gcactgcggc gctctccgt ccgcgggtgg ttgctgctgc tgccgctgct gctgggcctg 60
aacgcaggag ctgtcattga ctggcccaca gaggagggca aggaagtatg ggattatgtg 120
acgtccgca aggatgccta catgttcttg tggctctatt atgccacca ctctgcaag 180
aacttctcag aactgccct ggtcatgtgg cttcaggggc gtccaggcgg ttctagcact 240
ggatttgaa actttgagga aattgggcc cttgacagt atctcaaac acggaaaacc 300
acctggctcc aggtgccag tctcctatt gtggataat ccgtgggcac tgggttcagt 360
tatgtgaatg gtagtgggct ctatgccaag gacctggcta tgggtggctc agacatgatg 420
gttctcctga agaccttct cagttgccac aaagaattcc agacagttcc attctacatt 480
ttctcagagt cctatgg 497

```

<210> 191
<211> 175
<212> DNA
<213> Homo sapiens

<400> 191
atgttgaata ttttgcttat taactttggt tattgtcttc tccctcgatt agaattattag 60
ctacttgagt acaaggattt gagcctgtta cattcactgc tgaatttttag gctcctggaa 120
gatacccagc attcaataga gaccacacaa taaatatatg tcaaataaaa aaaaa 175

<210> 192
<211> 526
<212> DNA
<213> Homo sapiens

<400> 192
agtaaacatt attatTTTTT ttatatttgc aaaggaaaca tatctaattc ttcctataga 60
aagaacagta ttgctgtaat tccttttctt ttcttctca ttctctctgc cccttaaaag 120
attgaagaaa gagaaacttg tcaactcata tccacgttat ctagcaaagt acataagaat 180
ctatcactaa gtaatgtatc ctccagaatg tgttggttta ccagtgcac cccatattca 240
tcacaaaatt aaagcaagaa gtccatagta atttatttgc taatagtggg tttttaatgc 300
tcagagtttc tgagggtcaa ttttatcttt tcacttacaa gctctatgat cttaaataat 360
ttacttaatg tattttggtg tattttcttc aaattaatat tgggtgtcaa gactatatct 420
aatcctctg atcactttga gaaacaaact ttattaaat gtaaggcact tttctatgaa 480
ttttaaatat aaaaataaat attgttctga ttattactga aaaaaa 526

<210> 193
<211> 553
<212> DNA
<213> Homo sapiens

<220>
<221> unsure
<222> (290)
<223> n=A,T,C or G
<221> unsure
<222> (300)
<223> n=A,T,C or G
<221> unsure
<222> (411)
<223> n=A,T,C or G
<221> unsure
<222> (441)
<223> n=A,T,C or G

<400> 193
tccattgtgg tggaattcgc tctctggtaa aggcgtgcag gtgttgccg cggcctctga 60
gctgggatga gccgtgctcc cgggtggaagc aagggagccc agccggagcc atggccagta 120
cagtggtagc agttggactg accattgctg ctgcaggatt tgcaggccgt tacgttttgc 180
aagccatgaa gcatatggag cctcaagtaa aacaagtttt tcaaagccta ccaaaatctg 240
ccttcagtgg tggctattat agagggtgggt ttgaacccaa aatgacaaan cggaagcan 300
cattaatact aggtgtaagc cctactgcca ataaaggga aataagagat gctcatcgac 360
gaattatgct tttaaatcat cctgacaaag gaggatctcc ttatatagca nccaaaatca 420
atgaagctaa agatttacta naagggtcaag ctaaaaaatg aagtaaatgt atgatgaatt 480

ttaagttcgt attagtttat gtatatgagt actaagtttt tataataaaa tgcctcagag 540
ctacaatttt aaa 553

<210> 194

<211> 320

<212> DNA

<213> Homo sapiens

<400> 194

cccttcccaa tccatcagta aagaccccat ctgccttgtc catgccgttt cccaacaggg 60
atgtcacttg atatgagaat ctcaaatact aatgccttat aagcattcct tcctgtgtcc 120
attaagactc tgataattgt ctcccccca taggaatttc tcccaggaaa gaaatatatc 180
cccatctccg ttccatatca gaactaccgt ccccgatatt cccttcagag agattaaaga 240
ccagaaaaaa gtgagcctct tcatctgcac ctgtaatagt ttcagttcct attttcttcc 300
attgacccat atttatacct 320

<210> 195

<211> 320

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (203)

<223> n=A,T,C or G

<221> unsure

<222> (218)

<223> n=A,T,C or G

<400> 195

aagcatgacc tggggaaatg gtcagacctt gtattgtgtt tttggccttg aaagtagcaa 60
gtgaccagaa tctgccatgg caacaggctt taaaaaagac ccttaaaaag acactgtctc 120
aactgtgggtg ttagcaccag ccagctctct gtacatttgc tagctttagt ttttctaaga 180
ctgagtaaac ttcttatttt tanaaagggg aggctggntt gtaactttcc ttgtacttaa 240
ttgggtaaaa gtcttttcca caaaccacca tctattttgt gaactttggt agtcattctt 300
tatttggtaa attatgaact 320

<210> 196

<211> 357

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (36)

<223> n=A,T,C or G

<400> 196

atataaaata atacgaaact ttaaaaagca ttggantgtc agtatgttga atcagtagtt 60
tcactttaac tgtaaacaat ttcttaggac accatttggg ctagtcttct tgtaagtgtg 120
aatactacaa aaacttattt atactgttct tatgtcattt gttatattca tagatttata 180
tgatgatatg acatctggct aaaaagaaat tattgcaaaa ctaaccacta tgtacttttt 240
tataaatact gtatggacaa aaaatggcat tttttatatt aaattgttta gctctggcaa 300
aaaaaaaaa ttttaagagc tggactaat aaaggattat tatgactgtt aaaaaaa 357

<210> 197
 <211> 565
 <212> DNA
 <213> Homo sapiens

<220>
 <221> unsure
 <222> (27)
 <223> n=A,T,C or G

<400> 197
 tcagctgagt accatcagga tatttanccc ttttaagtgt gttttgggag tagaaaacta 60
 aagcaacaat acttcctctt gacagctttg attggaatgg gggtattaga tcattcacct 120
 tggctctaca ctttttagga tgcttggtga acataacacc acttataatg aacatccctg 180
 gttcctatat tttgggctat gtgggtagga attgttactt gttactgcag cagcagccct 240
 agaaaagtaag cccagggctt cagatctaag ttagtccaaa agctaaatga tttaaagtca 300
 agttgtaatg ctaggcataa gcactctata atacattaaa ttataggccg agcaattagg 360
 gaatgtttct gaaacattaa acttgtattt atgtcactaa aattctaaca caaacttaaa 420
 aaatgtgtct catacatatg ctgtactagg cttcatcatg catttctaaa tttgtgtatg 480
 atttgaatat atgaaagaat ttatacaaga gtgttattta aaattattaa aaataaatgt 540
 atataatttg tacctattgt aaaaa 565

<210> 198
 <211> 484
 <212> DNA
 <213> Homo sapiens

<400> 198
 tatgtaagta ttggtgtctg ctttaaaaaa ggagaccag acttcacctg tcctttttta 60
 acatttgaga acagtgttac tctgagcagt tgggccacct tcaccttacc cgacagctga 120
 ctgttgatg tgtccattgt cgcagtttg gctgttgcgc ggacaggaca ggacctccat 180
 tgggcgcagc agcaggtggc aggggtgtgg cttgaggtgg gtggcagcgt ctggctcctc 240
 tctctggtgc tttctgagag ggtctctaaa gcagagtgtg gttggcctgg gggaaggcag 300
 agcacgtatt tctccctct agtacctctg catttgtag tgtccctct ggctttctga 360
 agggcagcag actcttgagt atactgcaga ggacatgctt tatcagtagg tcctgagggc 420
 tccaggggct caactgacca agtaacacag aagttggggt atgtggccta tttgggtcgg 480
 aaac 484

<210> 199
 <211> 429
 <212> DNA
 <213> Homo sapiens

<220>
 <221> unsure
 <222> (77)
 <223> n=A,T,C or G
 <221> unsure
 <222> (88)
 <223> n=A,T,C or G
 <221> unsure
 <222> (134)
 <223> n=A,T,C or G
 <221> unsure
 <222> (151)

<223> n=A,T,C or G
 <221> unsure
 <222> (189)
 <223> n=A,T,C or G
 <221> unsure
 <222> (227)
 <223> n=A,T,C or G
 <221> unsure
 <222> (274)
 <223> n=A,T,C or G
 <221> unsure
 <222> (319)
 <223> n=A,T,C or G

<400> 199
 gcttatgttt tttgttttaa cttttgtttt ttaacattta gaatattaca ttttgtatta 60
 tacagtacct ttctcanaca ttttgtanaa ttcatttcgg cagctcacta ggattttgct 120
 gaacattaaa aagngtgata gcgatattag ngccaatcaa atggaaaaaa ggtagtctta 180
 ataaacaana cacaacgttt ttatacaaca tactttaaaa tattaanaaa actccttaat 240
 attgtttcct attaatgtatt attctttggg caanattttc tgatgtttt gatttttctt 300
 caatttagca tttgctttng gtttttttct ctatttagca ttctgttaag gcacaaaaac 360
 tatgtactgt atgggaaatg ttgtaaatat taccttttcc acatttttaa cagacaactt 420
 tgaatcaa 429

<210> 200
 <211> 279
 <212> DNA
 <213> Homo sapiens

<400> 200
 gcttttttga ggaattacag ggaagctcct ggaattgtac atggatatct ttatccctag 60
 ggggaaatca aggagctggg caccctaat tctttatgga agtgtttaaa actattttta 120
 tttttattaca agtattacta gtagtggt tctactctaa gatttcaaaa gtgcatttaa 180
 aatcatatcat gttccgcct gcaaatatat tggtattttg gtggagaaaa aaatagtata 240
 ttctacataa aaaattaaag atattaacta agaaaaaa 279

<210> 201
 <211> 569
 <212> DNA
 <213> Homo sapiens

<400> 201
 taggtcagta tttttagaaa ctcttaatag ctcatactct tgataccaaa agcagccctg 60
 attgttaaag cacacacctg cacaagaagc agtgatggtt gcattttacat ttcttgggtg 120
 cacaaaaaaa aattctcaaa aagcaaggac ttacgctttt tgcaagcct ttgagaagtt 180
 actggatcat aggaagctta taacaagaat ggaagattct taaataactc actttctttg 240
 gtatccagta acagtagatg ttcaaaatat gtagctgatt aataccagca ttgtgaacgc 300
 tgtacaacct tgtggttatt actaagcaag ttactactag ctctgaaaa gtagcttcat 360
 aattaatgtt atttatacac tgccttccat gacttttact ttgccctaag ctaatctcca 420
 aaatctgaaa tgctactcca atatcagaaa aaaaggggga ggtggaatta tatttctctg 480
 gattttaaga gtacagagaa tcatgcacat ctctgattag ttcatatatg tctagtgtgt 540
 aataaaagtc aaagatgaac tctcaaaaa 569

<210> 202
 <211> 501

<212> DNA

<213> Homo sapiens

<400> 202

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attaataggc ttaataattg ttggcaagga tccttttgct ttctttggca tgcaagctcc 60
tagcatctgg cagtggggcc aagaaaataa ggtttatgca tgtatgatgg ttttcttctt 120
gagcaacatg attgagaacc agtgtatgtc aacagggtgca tttgagataa ctttaaataga 180
tgtacctgtg tggcttaagc tggaatctgg tcaccttcca tccatgcaac aacttggtca 240
aattcttgac aatgaaatga agctcaatgt gcatatggat tcaatccac accatcgatc 300
atagcaccac ctatcagcac tgaaaactct tttgcattaa gggatcattg caagagcagc 360
gtgactgaca ttatgaaggc ctgtactgaa gacagcaagc tgtagtaca gaccagatgc 420
tttcttgga ggctcgttgc acctcttgga aaacctcaat gcaagatagc gtttcagtgc 480
tggcatattt tgaattctg c 501
```

<210> 203

<211> 261

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (36)

<223> n=A,T,C or G

<221> unsure

<222> (96)

<223> n=A,T,C or G

<400> 203

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gataaaatga atgagttctg tcatgattca ctattntata acttgcata cctttactgt 120
gttagctctt tgaatgttct tgaaatttta gactttcttt gtaaacaat gatatgtcct 180
tatcattgta taaaagctgt tatgtgcaac agtgtggaga ttccttgtct gatttaataa 240
aatacttaaa cactgaaaaa a 261
```

<210> 204

<211> 421

<212> DNA

<213> Homo sapiens

<400> 204

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agcatctttt ctacaacgtt aaaattgcag aagtagctta tcattaataa acaacaacaa 60
caacaataac aataaatcct aagtgtaaat cagttattct accccctacc aaggatatca 120
gcctgttttt tccctttttt ctcttgggaa taattgtggg cttcttccca aatttctaca 180
gcctctttcc tcttctcatg cttgagcttc cctgtttgca cgcatgctg tgcaggactg 240
gcttgtgtgc ttggactcgg ctccagggtg aagcatgctt tcccttgta ctgttggaga 300
aactcaaacc ttcaagccct aggtgtagcc attttgtcaa gtcataact gtatttttgt 360
actggcatta acaaaaaaag aagataaaat attgtacat taaacttta taaaacttta 420
a 421
```

<210> 205

<211> 460

<212> DNA

<213> Homo sapiens

<400> 205


```
tactctcaca atgaaggacc tggaaatgaaa aatctgtgtc taaacaagtc ctcttttagat 60
tttagtgcaa atccagagcc agcgtcggtt gcctcgagta attctttcat gggtagcttt 120
ggaaaagctc tcaggagacc tcacctagat gcctattcaa gctttggaca gccatcagat 180
tgtcagccaa gagcctttta tttgaaagct cattcttccc cagacttggc ctctgggtca 240
gaggaagatg ggaaagaaag gacagatttt caggaagaaa atcacatttg tacctttaaa 300
cagactttag aaaactacag gactccaaat tttcagtctt atgacttggc cacatagact 360
gaatgagacc aaaggaaaag cttaacatac tacctcaagg tgaactttta tttaaaagag 420
agagaatctt atgtttttta aatggagtta tgaattttaa 460
```

<210> 206

<211> 481

<212> DNA

<213> Homo sapiens

<400> 206

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tgtggtggaa ttcgggacgc cccagaccc tgactttttc ctgcgtgggc cgtctctccc 60
tgcggaagca gtgacctctg acccctggtg accttcgctt tgagtgcctt ttgaacgctg 120
gtcccgcggtg acttggtttt ctcaagctct gtctgtccaa agacgctccg gtcgaggtcc 180
cgctgccct ggggtgatac ttgaaccca gacgcccctc tgtctgtctg tgctcgaggg 240
cgcccttccc atctgctgc ccaccggag ctctttccgc cggcgaggg tcccaagccc 300
acctccgcc ctcagtcctg oggtgtgcgt ctgggcaagt cctgcacaca caatgcaagt 360
cctggcctcc gcgccgcc gccacgcga gccgtaccgc cgcgaactc tgttatttat 420
gggtgaccc cctggaggtg cctcggccc accggggcta tttattggtt aatttatttg 480
t 481
```

<210> 207

<211> 605

<212> DNA

<213> Homo sapiens

<400> 207

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accctttttg gattcagggc tcctcacaat taaaatgagt gtaatgaaac aagggtgaaa 60
tatagaagca tccctttgta tactgttttg ctacttacag tgtacttggc attgctttat 120
ctcaggatg tctcacgta ggatttctga gatcttaate taagctccaa agttgtctac 180
ttttttgatc ctagggtgct ccttttggtt tacagagcag ggtcacttga ttgctagct 240
gggtggcagaa ttggcaccat taccaggtc tgactgacca ccagtcagag gcactttatt 300
tgtatcatga aatgatttga aatcatttga aagcagcgaa gtctgataat gaatgccagc 360
tttcttctgt ctttgataac aaagactcca aatattctgg agaacctgga taaaagtgtg 420
aagggttaga ttgggatttg aagacaaaat tgtaggaaat cttacatttt tgcaataaca 480
aacattaatg aaagcaaac attataaaag taattttaat tcaccacata cttatcaatt 540
tcttgatgct tccaaatgac atctaccaga tatgggtttg tggacatctt tttctgttta 600
cataa 605
```

<210> 208

<211> 655

<212> DNA

<213> Homo sapiens

<400> 208

```
ggcgttggtc tggattcccg tcgtaactta aagggaact ttcacaatgt ccggagccct 60
tgatgtcctg caaatgaagg agggagatgt ccttaagttc cttgcagcag gaaccactt 120
aggtggcacc aatettgact tccagatgga acagtacatc tataaaagga aaagtgatgg 180
catctatata ataaatctca agaggacctg ggagaagctt ctgctggcag ctctgtgcaat 240
tggtgccatt gaaaacctg ctgatgtcag tggtatatcc tccaggaata ctggccagag 300
ggctgtgctg aagtttgctg ctgccactgg agccactcca attgctggcc gcttcaactc 360
```

tggaaccttc actaaccaga tccaggcagc ctcccgaggag ccacggcttc ttgtgggttac 420
tgacccccagg gctgaccacc agcctctcac ggaggcatct tatgttaacc tacctaccat 480
tgcgctgtgt aacacagatt ctctctcgcg ctatgtggac attgccatcc catgcaacaa 540
caaggaggct cactcagtgg gtttgatgtg gtggatgctg gctcgggaag ttctgcgcat 600
gcgtggcacc atttcccgctg aacacccatg ggaggatcat cctgatctgt acttc 655

<210> 209

<211> 621

<212> DNA

<213> Homo sapiens

<400> 209

catttagaac atgggttatca tccaagacta ctctaccctg caacattgaa ctcccaagag 60
caaatccaca ttctcttga gttctgcagc ttctgtgtaa atagggcagc tgcgtcttat 120
gccgtagaat cacatgatct gaggaccatt catggaagct gctaaatagc ctagtctggg 180
gagtccttcca taaagttttg catggagcaa acaaacagga ttaaactagg ttgtgttcct 240
tcagccctct aaaagcatag ggcttagcct gcaggcttcc ttgggctttc tctgtgtgtg 300
tagttttgta aacactatag catctgttaa gatccagtgt ccatggaaac cttcccacat 360
gccgtgactc tggactatat cagtttttgg aaagcagggt tcctctgcct gctaacaagc 420
ccacgtggac cagtctgaat gtctttcctt tacacctatg tttttaataa gtcaaaactc 480
aagaaacaat ctaaacaagt ttctgttgca tatgtgtttg tgaacttgta tttgtattta 540
gtaggcttct atattgcatt taacttgttt ttgtaactcc tgattcttcc ttttcggata 600
ctattgatga ataaagaaat t 621

<210> 210

<211> 533

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (20)

<223> n=A,T,C or G

<221> unsure

<222> (21)

<223> n=A,T,C or G

<221> unsure

<222> (61)

<223> n=A,T,C or G

<400> 210

cgccttgggg agccggcggn ngagtccggg acgtggagac cgggggtccc ggcagccggg 60
nggcccgcgg gccaggggtg gggatgcacc gccgcggggt gggagctggc gccatcgcca 120
agaagaaact tgagaggcc aagtataagg agcaggggac ggtcttggct gaggaccagc 180
tagcccagat gtcaaagcag ttggacatgt tcaagaccaa cctggaggaa tttgccagca 240
aacacaagca ggagatccgg aagaatcctg agttccgtgt gcagttccag gacatgtgtg 300
caaccattgg cgtggatccg ctggcctctg gaaaaggatt ttggtctgag atgctgggcg 360
tgggggactt ctattacgaa ctaggtgtcc aaattatcga agtgtgcctg gcgctgaagc 420
atcggaatgg aggtctgata actttggagg aactacatca acaggtgttg aagggaaggg 480
gcaagttcgc ccaggatgtc agtcaagatg acctgatcag agccatcaag aaa 533

<210> 211

<211> 451

<212> DNA

<213> Homo sapiens

<400> 211
 ttagcttgag ccgagaacga ggcgagaaag ctggagaccg aggagaccgc ctagagcgga 60
 gtgaacgggg aggggaccgt ggggaccggc ttgatcgtgc gcggacacct gctaccaagc 120
 ggagcttcag caaggaagtg gaggagcgga gtagagaacg gccctcccag cctgaggggc 180
 tgcgcaaggc agctagcctc acggaggatc gggaccgtgg gcgggatgcc gtgaagcgag 240
 aagctgccct acccccagtg agccccctga agcggtctct ctctgaggag gagttagaga 300
 agaaatccaa ggctatcatt gaggaatatt tccatctcaa tgacatgaaa gaggcagtcc 360
 agtgcggtga ggagctggcc tcacctctct tgctcttcat ctttgtacgg catggtgtcg 420
 agtctacgct ggagcgcgct gccattgctc g 451

<210> 212
 <211> 471
 <212> DNA
 <213> Homo sapiens

<220>
 <221> unsure
 <222> (54)
 <223> n=A,T,C or G

<400> 212
 gtgattattc ttgatcaggg agaagatcat ttagatttgt tttgcattcc ttanaatgga 60
 gggcaacatt ccacagctgc cctggctgtg atgagtgtcc ttgcaggggc cggagtagga 120
 gcactggggg gggggcgga ttgggggttac tcgatgtaag ggattccttg ttgttgtgtt 180
 gagatccagt gcagttgtga tttctgtgga tccagcttg gttccaggaa ttttgtgtga 240
 ttggcttaaa tccagttttc aatcttcgac agctgggctg gaacgtgaac tcagtagctg 300
 aacctgtctg acccggtcac gttcttgat cctcagaact ctttgcctct gtcggggtgg 360
 ggggtgggaac tcacgtgggg agcggtggct gagaaaatgt aaggattctg gaatacatat 420
 tccatgggac tttccttccc tctcctgctt cctcttttcc tgctccctaa c 471

<210> 213
 <211> 511
 <212> DNA
 <213> Homo sapiens

<220>
 <221> unsure
 <222> (27)
 <223> n=A,T,C or G
 <221> unsure
 <222> (63)
 <223> n=A,T,C or G
 <221> unsure
 <222> (337)
 <223> n=A,T,C or G
 <221> unsure
 <222> (442)
 <223> n=A,T,C or G

<400> 213
 ctaattagaa acttgctgta ctttttnttt tcttttaggg gtcaaggacc ctctttatag 60
 ctncatttgc cctacaataa attattgcag cagtttgcaa tactaaaata ttttttatag 120
 actttatatt tttccttttg ataaagggat gctgcatagt agagttggtg taattaaact 180
 atctcagcgg tttccctgct ttcccttctg ctccatattg ctcattgtcc ttccagggag 240

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ctcttttaat cttaaagttc tacatttcat gctcttagtc aaattctggt accttttttaa 300
taactcttcc cactgcatat ttccatcttg aattggnggt tctaaattct gaaactgtag 360
ttgagataca gctattttaat atttctggga gatgtgcac cctcttcttt gtggttgccc 420
aaggttgttt tgcgtaactg anactccttg atatgcttca gagaatttag gcaaactg 480
gccatggccg tgggagtact gggagtaaaa t 511

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<210> 214

<211> 521

<212> DNA

<213> Homo sapiens

<400> 214

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agcattgcc aataatccct aattttccac taaaaatata atgaaatgat gttaagcttt 60
ttgaaaagtt taggttaaac ctactgttgt tagattaatg tatttggtgc ttccctttat 120
ctggaatgtg gcattagctt ttttatttta accctcttta attcttattc aattccatga 180
cttaagggtg gagagctaaa cactgggatt ttgggataac agactgacag ttttgcataa 240
ttataatcgg cattgtacat agaaaggata tggctacctt ttgttaaate tgcactttct 300
aaatatcaaa aaagggaat gaagtataaa tcaatttttg tataatctgt ttgaaacatg 360
agtttttatt gcttaatttt agggctttgc cccttttctg taagtctctt gggatcctgt 420
gtagaagctg ttctcattaa acaccaaaca gttaagtcca ttctctggta ctagtacaa 480
attcggtttc atattctact taacaattta aataaactga a 521

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<210> 215

<211> 381

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (17)

<223> n=A,T,C or G

<221> unsure

<222> (20)

<223> n=A,T,C or G

<221> unsure

<222> (60)

<223> n=A,T,C or G

<221> unsure

<222> (61)

<223> n=A,T,C or G

<221> unsure

<222> (365)

<223> n=A,T,C or G

<400> 215

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ncatcacacc ccgggaggag ccgagctgc gcagccggc cccagtcacc atcacgcaa 120
ccatgagcag cgaggccgag acccagcagc cgcccgccgc ccccccgcc gcccccgccc 180
tcagcgccgc cgacaccaag cccggcacta cgggcagcgg cgaggggagc ggtggcccg 240
ggcgccctcac atcgggggcg cctgccggcg gggacaagaa ggtcatcgca acgaaggttt 300
tgggaacagt aaaatggttc aatgtaagga acggatatgg ttcatcaac aggaatgaca 360
ccaangaaga tgtatttgta c 381

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<210> 216

<211> 425

<212> DNA

<213> Homo sapiens

<400> 216

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ttactaacta ggtcattcaa ggaagtcaag ttaacttaaa catgtcacct aaatgcactt 60
gatgggtgtg aaatgtccac cttcttaaat ttttaagatg aacttagttc taaagaagat 120
aacaggccaa tctgaaggt actcctgtt tgetgcagaa tgtcagatat tttggatgtt 180
gcataagagt cctatttgcc ccagttaatt caacttttgt ctgcctgttt tgtggactgg 240
ctggctctgt tagaactctg tccaaaaagt gcatggaata taacttgtaa agcttccac 300
aattgacaat atatatgcat gtgtttaaac caaatccaga aagcttaaac aatagagctg 360
cataatagta tttattaaag aatcacaact gtaaacatga gaataactta aggattctag 420
ttagg                                     425

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<210> 217

<211> 181

<212> DNA

<213> Homo sapiens

<400> 217

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gagaaaccaa atgatagggt gtagagcctg atgactccaa acaaagccat caccgcatt 60
cttctcctt cttctgtgtc tacagctcca agggcccttc accttcattg ctgaaatgga 120
actttggctt tttcagtgga agaatatgtt gaaggtttca ttttgttcta gaaaaaaaaa 180
a                                     181

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<210> 218

<211> 405

<212> DNA

<213> Homo sapiens

<400> 218

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caggccttcc agttcactga caaacatggg gaagtgtgcc cagctggctg gaaacctggc 60
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gcgctgggct gtttttagtgc caggctgcgg tgggcagcca tgagaacaaa acctcttctg 180
tatttttttt ttccattagt aaaacacaag acttcagatt cagccgaatt gtggtgtctt 240
acaaggcagg cctttcttac agggggtgga gagaccagcc tttcttctt tggtaggaat 300
ggcctgagtt ggcgttgtgg gcaggctact ggtttgtatg atgtattagt agagcaaccc 360
attaatcttt tgtagtttgt attaaacttg aactgagaaa aaaaa 405

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<210> 219

<211> 216

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (207)

<223> n=A,T,C or G

<221> unsure

<222> (210)

<223> n=A,T,C or G

<400> 219

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ttaatttacc atgtaaaatt gctgtaaagc ataattgtga cagattttct gttcaaatat 120
tcaattgtaa acttcttgtt aagactgtta cgtttctatt gcttttgtat gggatattgc 180

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aaaaataaaa aggaaagaac cctcttnaan aaaaaa

216

<210> 220

<211> 380

<212> DNA

<213> Homo sapiens

<400> 220

cttacaaatt gcccccatgt gtaggggaca cagaaccctt tgagaaaact tagatttttg 60
tctgtacaaa gtctttgcct ttttccttct tcattttttt ccagtacatt aaatttgtca 120
atttcatctt tgagggaaac tgattagatg ggttggtgtt gtgttctgat ggagaaaaca 180
gcacccaag gactcagaag atgattttta cagttcagaa cagatgtgtg caatattggt 240
gcatgtaata atgttgagtg gcagtcaaaa gtcattgatt ttatcttagt tcttcattac 300
tgcattgaaa aggaaaacct gtctgagaaa atgcctgaca gtttaattta aaactatggt 360
gtaagtcttt gacaaaaaaa 380

<210> 221

<211> 398

<212> DNA

<213> Homo sapiens

<400> 221

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tgtatattta atgaatgaac atgtacaatt tgccactggg aggagggtcc tttttgttgg 120
gtgagtctgc aagtgaattt cactgatgtt gatattcatt gtgtgtagtt ttatttcggt 180
cccagcccg tttcctttta ttttggagct aatgccagct gcgtgtctag ttttgagtgc 240
agtaaaatag aatcagcaaa tcactcttat ttttcactct tttccggtat tttttgggtt 300
gtttctgtgg gagcagtgtt caccaactct tcctgtatat tgcctttttg ctggaaaatg 360
ttgtatgttg aataaaattt tctataaaaa ttaaaaaa 398

<210> 222

<211> 301

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (49)

<223> n=A,T,C or G

<221> unsure

<222> (64)

<223> n=A,T,C or G

<400> 222

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taanaacttg aaacttgtaa actgagatgt ctgtagcttt tttgcccac tgtagtgtat 120
gtgaagattt caaaacctga gagcactttt tctttgttta gaattatgag aaaggcacta 180
gatgacttta ggatttgcatt ttttcctttt attgcctcat ttcttgtgac gccttgttgg 240
ggagggaaat ctgtttattt tttcctacaa ataaaaagct aagattctat atcgcaaaaa 300
a 301

<210> 223

<211> 200

<212> DNA

<213> Homo sapiens

<400> 223

gtaagtgtt aggaagaaac tttgcaaaca tttaatgagg atacactgtt cattttttaa 60
 attccttcac actgtaattt aatgtgtttt atattctttt gtagtaaaac aacataactc 120
 agatttctac aggagacagt ggttttattt ggattgtctt ctgtaatagg tttcaataaa 180
 gctggatgaa cttaaaaaaa 200

<210> 224

<211> 385

<212> DNA

<213> Homo sapiens

<400> 224

gaaagggttg atccggactc aaagaaagca aaggagtgtg agccgccatc tgctggagca 60
 gctgtaactg caagacctgg acaagagatt cgtcagcgaa ctgcagctca aagaaacctt 120
 tctccaacac cagcaagccc taaccagggc cctcctccac aagttccagt atctcctgga 180
 ccaccaaagg acagttctgc ccttggtgga cccccagaaa ggactgttac tccagcccta 240
 tcatcaaagt tgttaccaag acatcttgga tccccgcta cttcagtgcc tggaaatgggt 300
 aaacagagca cttaatgtta tttacagttt atattgtttt ctctggttac caataaaacg 360
 ggccattttc aggtggtaaa aaaaa 385

<210> 225

<211> 560

<212> PRT

<213> Homo sapien

<400> 225

Met	Glu	Cys	Leu	Tyr	Tyr	Phe	Leu	Gly	Phe	Leu	Leu	Leu	Ala	Ala	Arg
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Leu	Pro	Leu	Asp	Ala	Ala	Lys	Arg	Phe	His	Asp	Val	Leu	Gly	Asn	Glu
			20					25					30		
Arg	Pro	Ser	Ala	Tyr	Met	Arg	Glu	His	Asn	Gln	Leu	Asn	Gly	Trp	Ser
			35				40					45			
Ser	Asp	Glu	Asn	Asp	Trp	Asn	Glu	Lys	Leu	Tyr	Pro	Val	Trp	Lys	Arg
	50					55					60				
Gly	Asp	Met	Arg	Trp	Lys	Asn	Ser	Trp	Lys	Gly	Gly	Arg	Val	Gln	Ala
65					70					75				80	
Val	Leu	Thr	Ser	Asp	Ser	Pro	Ala	Leu	Val	Gly	Ser	Asn	Ile	Thr	Phe
				85					90					95	
Ala	Val	Asn	Leu	Ile	Phe	Pro	Arg	Cys	Gln	Lys	Glu	Asp	Ala	Asn	Gly
			100					105					110		
Asn	Ile	Val	Tyr	Glu	Lys	Asn	Cys	Arg	Asn	Glu	Ala	Gly	Leu	Ser	Ala
	115						120					125			
Asp	Pro	Tyr	Val	Tyr	Asn	Trp	Thr	Ala	Trp	Ser	Glu	Asp	Ser	Asp	Gly
	130					135					140				
Glu	Asn	Gly	Thr	Gly	Gln	Ser	His	His	Asn	Val	Phe	Pro	Asp	Gly	Lys
145					150					155				160	
Pro	Phe	Pro	His	His	Pro	Gly	Trp	Arg	Arg	Trp	Asn	Phe	Ile	Tyr	Val
			165						170					175	
Phe	His	Thr	Leu	Gly	Gln	Tyr	Phe	Gln	Lys	Leu	Gly	Arg	Cys	Ser	Val
			180					185					190		
Arg	Val	Ser	Val	Asn	Thr	Ala	Asn	Val	Thr	Leu	Gly	Pro	Gln	Leu	Met
		195					200					205			
Glu	Val	Thr	Val	Tyr	Arg	Arg	His	Gly	Arg	Ala	Tyr	Val	Pro	Ile	Ala

210		215		220
Gln Val Lys Asp Val Tyr Val Val Thr Asp Gln Ile Pro Val Phe Val				
225		230		240
Thr Met Phe Gln Lys Asn Asp Arg Asn Ser Ser Asp Glu Thr Phe Leu				
	245		250	255
Lys Asp Leu Pro Ile Met Phe Asp Val Leu Ile His Asp Pro Ser His				
	260		265	270
Phe Leu Asn Tyr Ser Thr Ile Asn Tyr Lys Trp Ser Phe Gly Asp Asn				
	275		280	285
Thr Gly Leu Phe Val Ser Thr Asn His Thr Val Asn His Thr Tyr Val				
	290		295	300
Leu Asn Gly Thr Phe Ser Leu Asn Leu Thr Val Lys Ala Ala Ala Pro				
305		310		320
Gly Pro Cys Pro Pro Pro Pro Pro Pro Arg Pro Ser Lys Pro Thr				
	325		330	335
Pro Ser Leu Gly Pro Ala Gly Asp Asn Pro Leu Glu Leu Ser Arg Ile				
	340		345	350
Pro Asp Glu Asn Cys Gln Ile Asn Arg Tyr Gly His Phe Gln Ala Thr				
	355		360	365
Ile Thr Ile Val Glu Gly Ile Leu Glu Val Asn Ile Ile Gln Met Thr				
	370		375	380
Asp Val Leu Met Pro Val Pro Trp Pro Glu Ser Ser Leu Ile Asp Phe				
385		390		400
Val Val Thr Cys Gln Gly Ser Ile Pro Thr Glu Val Cys Thr Ile Ile				
	405		410	415
Ser Asp Pro Thr Cys Glu Ile Thr Gln Asn Thr Val Cys Ser Pro Val				
	420		425	430
Asp Val Asp Glu Met Cys Leu Leu Thr Val Arg Arg Thr Phe Asn Gly				
	435		440	445
Ser Gly Thr Tyr Cys Val Asn Leu Thr Leu Gly Asp Asp Thr Ser Leu				
	450		455	460
Ala Leu Thr Ser Thr Leu Ile Ser Val Pro Asp Arg Asp Pro Ala Ser				
465		470		480
Pro Leu Arg Met Ala Asn Ser Ala Leu Ile Ser Val Gly Cys Leu Ala				
	485		490	495
Ile Phe Val Thr Val Ile Ser Leu Leu Val Tyr Lys Lys His Lys Glu				
	500		505	510
Tyr Asn Pro Ile Glu Asn Ser Pro Gly Asn Val Val Arg Ser Lys Gly				
	515		520	525
Leu Ser Val Phe Leu Asn Arg Ala Lys Ala Val Phe Phe Pro Gly Asn				
	530		535	540
Gln Glu Lys Asp Pro Leu Leu Lys Asn Gln Glu Phe Lys Gly Val Ser				
545		550		560

<210> 226

<211> 9

<212> PRT

<213> Homo sapien

<400> 226

Ile Leu Ile Pro Ala Thr Trp Lys Ala

1

5

<210> 227

<211> 9

<212> PRT

<213> Homo sapien

<400> 227

Phe Leu Leu Asn Asp Asn Leu Thr Ala

1

5

<210> 228

<211> 9

<212> PRT

<213> Homo sapien

<400> 228

Leu Leu Gly Asn Cys Leu Pro Thr Val

1

5

<210> 229

<211> 10

<212> PRT

<213> Homo sapien

<400> 229

Lys Leu Leu Gly Asn Cys Leu Pro Thr Val

1

5

10

<210> 230

<211> 10

<212> PRT

<213> Homo sapien

<400> 230

Arg Leu Thr Gly Gly Leu Lys Phe Phe Val

1

5

10

<210> 231

<211> 9

<212> PRT

<213> Homo sapien

<400> 231

Ser Leu Gln Ala Leu Lys Val Thr Val

1

5

<210> 232

<211> 20

<212> PRT

<213> Homo sapiens

<400> 232

Ala Gly Ala Asp Val Ile Lys Asn Asp Gly Ile Tyr Ser Arg Tyr Phe

5

10

15

Phe Ser Phe Ala

20

<210> 233
<211> 21
<212> PRT
<213> Homo sapiens

<400> 233
Phe Phe Ser Phe Ala Ala Asn Gly Arg Tyr Ser Leu Lys Val His Val
5 10 15

Asn His Ser Pro Ser
20

<210> 234
<211> 20
<212> PRT
<213> Homo sapiens

<400> 234
Phe Leu Val Thr Trp Gln Ala Ser Gly Pro Pro Glu Ile Ile Leu Phe
5 10 15

Asp Pro Asp Gly
20

<210> 235
<211> 20
<212> PRT
<213> Homo sapiens

<400> 235
Leu Gln Ser Ala Val Ser Asn Ile Ala Gln Ala Pro Leu Phe Ile Pro
5 10 15

Pro Asn Ser Asp
20

<210> 236
<211> 20
<212> PRT
<213> Homo sapiens

<400> 236
Ile Gln Asp Asp Phe Asn Asn Ala Ile Leu Val Asn Thr Ser Lys Arg
5 10 15

Asn Pro Gln Gln
20

<210> 237

<211> 21
<212> PRT
<213> Homo sapiens

<400> 237
Arg Asn Ser Leu Gln Ser Ala Val Ser Asn Ile Ala Gln Ala Pro Leu
 5 10 15
Phe Ile Pro Pro Asn
 20

<210> 238
<211> 20
<212> PRT
<213> Homo sapiens

<400> 238
Thr His Glu Ser His Arg Ile Tyr Val Ala Ile Arg Ala Met Asp Arg
 5 10 15
Asn Ser Leu Gln
 20

<210> 239
<211> 20
<212> PRT
<213> Homo sapiens

<400> 239
Arg Asn Pro Gln Gln Ala Gly Ile Arg Glu Ile Phe Thr Phe Ser Pro
 5 10 15
Gln Ile Ser Thr
 20

<210> 240
<211> 21
<212> PRT
<213> Homo sapiens

<400> 240
Gly Gln Ala Thr Ser Tyr Glu Ile Arg Met Ser Lys Ser Leu Gln Asn
 5 10 15
Ile Gln Asp Asp Phe
 20

<210> 241
<211> 20
<212> PRT
<213> Homo sapiens

<400> 241

Glu Arg Lys Trp Gly Phe Ser Arg Val Ser Ser Gly Gly Ser Phe Ser
5 10 15

Val Leu Gly Val
20

<210> 242

<211> 20

<212> PRT

<213> Homo sapiens

<400> 242

Gly Ser His Ala Met Tyr Val Pro Gly Tyr Thr Ala Asn Gly Asn Ile
5 10 15

Gln Met Asn Ala
20

<210> 243

<211> 20

<212> PRT

<213> Homo sapiens

<400> 243

Val Asn His Ser Pro Ser Ile Ser Thr Pro Ala His Ser Ile Pro Gly
5 10 15

Ser His Ala Met
20

<210> 244

<211> 20

<212> PRT

<213> Homo sapiens

<400> 244

Ala Val Pro Pro Ala Thr Val Glu Ala Phe Val Glu Arg Asp Ser Leu
5 10 15

His Phe Pro His
20

<210> 245

<211> 20

<212> PRT

<213> Homo sapiens

<400> 245

Lys Pro Gly His Trp Thr Tyr Thr Leu Asn Asn Thr His His Ser Leu

117

5

10

15

Gln Ala Leu Lys
20

<210> 246
<211> 20
<212> PRT
<213> Homo sapiens

<400> 246
Asn Leu Thr Phe Arg Thr Ala Ser Leu Trp Ile Pro Gly Thr Ala Lys
5 10 15

Pro Gly His Trp
20

<210> 247
<211> 20
<212> PRT
<213> Homo sapiens

<400> 247
Leu His Phe Pro His Pro Val Met Ile Tyr Ala Asn Val Lys Gln Gly
5 10 15

Phe Tyr Pro Ile
20

<210> 248
<211> 20
<212> PRT
<213> Homo sapiens

<400> 248
Pro Glu Thr Gly Asp Pro Val Thr Leu Arg Leu Leu Asp Asp Gly Ala
5 10 15

Gly Ala Asp Val
20

<210> 249
<211> 20
<212> PRT
<213> Homo sapiens

<400> 249
Gly Phe Tyr Pro Ile Leu Asn Ala Thr Val Thr Ala Thr Val Glu Pro
5 10 15

Glu Thr Gly Asp

20

<210> 250
 <211> 20
 <212> PRT
 <213> Homo sapiens

<400> 250
 Phe Asp Pro Asp Gly Arg Lys Tyr Tyr Thr Asn Asn Phe Ile Thr Asn
 5 10 15

Leu Thr Phe Arg
 20

<210> 251
 <211> 20
 <212> PRT
 <213> Homo sapiens

<400> 251
 Leu Gln Ala Leu Lys Val Thr Val Thr Ser Arg Ala Ser Asn Ser Ala
 5 10 15

Val Pro Pro Ala
 20

<210> 252
 <211> 153
 <212> PRT
 <213> Homo sapien

<400> 252
 Met Ala Ser Val Arg Val Ala Ala Tyr Phe Glu Asn Phe Leu Ala Ala
 1 5 10 15
 Trp Arg Pro Val Lys Ala Ser Asp Gly Asp Tyr Tyr Thr Leu Ala Val
 20 25 30
 Pro Met Gly Asp Val Pro Met Asp Gly Ile Ser Val Ala Asp Ile Gly
 35 40 45
 Ala Ala Val Ser Ser Ile Phe Asn Ser Pro Glu Glu Phe Leu Gly Lys
 50 55 60
 Ala Val Gly Leu Ser Ala Glu Ala Leu Thr Ile Gln Gln Tyr Ala Asp
 65 70 75 80
 Val Leu Ser Lys Ala Leu Gly Lys Glu Val Arg Asp Ala Lys Ile Thr
 85 90 95
 Pro Glu Ala Phe Glu Lys Leu Gly Phe Pro Ala Ala Lys Glu Ile Ala
 100 105 110
 Asn Met Cys Arg Phe Tyr Glu Met Lys Pro Asp Arg Asp Val Asn Leu
 115 120 125
 Thr His Gln Leu Asn Pro Lys Val Lys Ser Phe Ser Gln Phe Ile Ser
 130 135 140
 Glu Asn Gln Gly Ala Phe Lys Gly Met
 145 150

<210> 253
 <211> 462
 <212> DNA
 <213> Homo sapien

<400> 253
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 aaagcctctg atggagatta ctacaccttg gctgtaccga tgggagatgt accaatggat 120
 ggtatctctg ttgctgatat tggagcagcc gtctctagca tttttaattc tccagaggaa 180
 ttttttagca aggcgtggg gctcagtga gaagcactaa caatacagca atatgctgat 240
 gttttgtcca aggccttggg gaaagaagtc cgagatgcaa agattacccc ggaagctttc 300
 gagaagctgg gattccctgc agcaaaggaa atagccaata tgtgtcgttt ctatgaaatg 360
 aagccagacc gagatgtcaa tctcacccac caactaaatc ccaaagtcaa aagcttcagc 420
 cagtttatct cagagaacca gggagccttc aagggcattg ag 462

<210> 254
 <211> 8031
 <212> DNA
 <213> Homo sapien

<400> 254
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 cagcgtgacc gctacacttg ccagcgccct agcgcgcgt cctttcgctt tcttcccttc 120
 ctttctcgcc acgttcgcgc gctttccccc tcaagctcta aatcgggggc tccctttagg 180
 gtcccgattt agtgctttac ggcacctga ccccaaaaaa cttgattagg gtgatggttc 240
 acgtagtggg ccatcgccct gatagacggg ttttcgcctt ttgacgttgg agtccacgtt 300
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 acaaaaattt aacgcgaatt ttaacaaaat attaacgttt acaatttcag gtggcacttt 480
 tcgggggaaat gtgcgcggaa cccctatttg tttatttttc taaatacatt caaatatgta 540
 tccgctcatg aattaattct tagaaaaact catcgagcat caaatgaaac tgcaatttat 600
 tcatatcagg attatcaata ccatattttt gaaaaagccg tttctgtaat gaaggagaaa 660
 actcaccgag gcagttccat aggatggcaa gatectggta tcgggtctgcg attccgactc 720
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<210> 255

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 255

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agtccanagg acggagaaga cgaggaagag	gaggagcagt	tggttctggg	ggaattatca	120
ggaattattg attcagactt cctctcaaaa	tgtgaaaata	aatgcaaggt	tttgggcatt	180
gacactgaga ggcccattct gcaagtggac	agctgtgtct	ttgctgggga	gtatgaagac	240
actctangga cctgtgttat atttgaagaa	aatgntnaac	atgctgatac	agaaggcaat	300
aataaaacag tgctaaaata taaatgccat	acaatgaaga	agctcagcat	gacaagaact	360
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<210> 256

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 256

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ggccgaggat aaggagtga tgcccgtcac	caacttgggc	cgcttgncca	aggacatgaa	180
nancaagccc ctgnaggaga tctatntctt	cttccctgcc	ccattaagga	atcaagagat	240
catttgattt cttcctgggg gcctctctca	aggatnaggt	ttttgaagat	tatgccagt	300
canaaaannan acccggttgc ccngtccatc	tncacccaac	ncttccaagg	gcnatttttg	360
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<210> 257

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 257

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ctctcagccc tgaggatatac agaatcattt	gcctcagact	gctgttggat	tttaaaattt	120
ttaaaataac tgctaagtaa tttgctatgt	cttctccac	actatcaata	tgctgtcttc	180
taacaggctc ccacttttct tttaatgtgc	tgttatgagc	tttgacatg	agataaccgt	240
gcctgttcag agtgtctaca gtaagagctg	gacaaactct	ggagggacac	agtctttgag	300
acagctcttt tggttgcttt ccacttttct	gaaaggttca	cagtaacctt	ctagataata	360
gaaactccca gttaaagcct angctancaa	ttttttttag	t		401

<210> 258

<211> 401

<212> DNA

<213> Homo sapien

<400> 258

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tctgtggagg agcagcagta gtcggagggt gcaggatatt agaaatggct actccccagt	180	
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gctactatga tatcttaggt gtgccaaaat cggcatcaga gcgccaaatc aagaaggcct	300	-
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<210> 259

<211> 401

<212> DNA

<213> Homo sapien

<400> 259

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acagctcagg ctacagaag ggcagaaact ttgattttca gccgccatgc tgtgattgcc	180
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gttcctatc accaactgga cattcctgtt gataacocaa tcgagagcaa taacattttt	360
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<210> 260

<211> 363

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (363)

<223> n = A,T,C or G

<400> 260

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cagggtggggg ctgggggtggg gcatggagag ccttttngat cccccaggcc accctgctct	180
cgctggngctg ttgaaaccca ctccatggct tectgccact gcagttggggc ccagggtggtg	240
cttattnctg gaatgcaagt ggctgtggct tggagcctcc cctctggnnn anggaaannn	300
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<210> 261

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (401)

<223> n = A,T,C or G

<400> 261

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cttccctgga tttgatgagc gggctgatgc anaaactctt cggaaggcta tgaaaggctt 180
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ggaaatctct gcagctttta agactctgtt tggcagggat cttctggatg acctgaaatc 300
agaactaact ggaaaatttg aaaaattaat tgtggctctg atgaaaccct ctcggcttta 360
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<210> 262
<211> 401
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(401)
<223> n = A,T,C or G

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<400> 262
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agtttataac atgaagaata ttgtaccatt atacattttc attctcgatc tcataagaaa 180
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tcaactcaaa aattatgntg catagtttta ttttgaattt aggttttggg actacttttt 300
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<210> 263
<211> 401
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(401)
<223> n = A,T,C or G

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<400> 263
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gcggcggttg cggttagggc ggccggaat aaaggggccc cggccgggtg atgcggtgac 180
cactgcggca ggcccaggag ctgagtgggc ccgggccc agcccgtecc gncggaccgg 240
ctttctcaa ctctccatct tctctgccc accgagatcg ccgaggcggn ctcaggctcc 300
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cctccacca tggctctgaa ganaatccac aaggaattga a 401

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<210> 264
<211> 401
<212> DNA
<213> Homo sapien

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<400> 264
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actttggcca gcattgacct tcaaagtcag atggaacca ggaccatcc aacttggctg 180
cttcacattt teatccctc ctgcacatt gctttcattt tcatagccac agtgatagcc 240
ctaagaaaac aactctgtca aaagctgtat tcttcaaaag acacaacaaa aagacctgtc 300

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accacaacaa agaggggaagt gaacagtgct gtgaatctga acctgtggtc ttgggagcca 360
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<210> 265

<211> 271

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(271)

<223> n = A,T,C or G

<400> 265

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gttagaagtt tctagatctg gccgggcgca gtggctcaca cctgtaatcc cagcacttta 180
ggaggctgag gcaggcgat catgaggtca ggagatcgag accgtcctgg ctaacacagt 240
gaaaccccgct ctctactaaa aatacaaaaa a 271

<210> 266

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 266

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tctattttaa atgactttct ggatttttaa aaatttcttt aaatacaatc atttttgtaa 180
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<210> 267

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 267

gaagaggcat cactgatcc cggagacctt tggagttaag aggcggcgga agcgagggcc 60
tgtggagtgc gatcctcttc ggggtgagcc agggtcggcg cgcgcggctg tctcanaact 120
catgcagctg ttcccgcgag gctgtttga ggacgcgctg ccgcccatcg tgctgaggag 180
ccaggtgtac agccttgtgc ctgacaggac cgtggccgac cggcagctga aggagcttca 240
agagcanggg gagacaaaat cgtccagctg ggcttcnact tggatgccca tggaanttat 300

tctttcnctt ganggactta cnnngggaccc aagaancctt tncaaggggc ccttngtgga 360
 tgggncccg aaccccnnta tttgcccttg ggggggncca a 401

<210> 268

<211> 223

<212> DNA

<213> Homo sapien

<400> 268

tgcctatgtt ggccaggctg gtcttgaact cctgacttta agtgatccac ccgcctcaac 60
 ctcccaaagt gctgggatta cagggtgtgag ccaccgcgc tggcctgata catactttta 120
 gaatcaagta gtcacgcact ttttctgttc atttttctaa aaagtaaata tacaaatgtt 180
 ttgttttttg ttttttttgt ttgtttgttt ctgttttttt ttt 223

<210> 269

<211> 401

<212> DNA

<213> Homo sapien

<400> 269

actatgtaaa ccacattgta ctttttttta ctttggcaac aaatatttat acatacaaga 60
 tgctagtcca tttgaatatt tctcccaact tatccaagga tctccagctc taacaaaatg 120
 gtttattttt atttaaagt caatagttgt tttttaaagt ccaaatcaga ggtgcaggcc 180
 accagttaaa tgccgtctat caggttttgt gccttaagag actacagagt caaagctcat 240
 ttttaaagga gtaggacaaa gttgtcacag gtttttggtg ttgtttttat tgcccccaa 300
 attacatgtt aatttccatt tatatcaggg attctattta cttgaagact gtgaagttgc 360
 cattttgtct cattgttttc tttgacataa ctaggatcca t 401

<210> 270

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (401)

<223> n = A, T, C or G

<400> 270

tggtctgtga ttcacctcag cactgcttgg tatctgcacc ctacctctct ttagaggctg 60
 ccttgtcaac tgaaaaatgc acctgacttc gagcaagact ctttcccttag gttctggatc 120
 tgtttgagcc ccatggcact gagctggaat ctgagggtct tgttccaagg atgtgatgat 180
 gtggggagaat gttctttgaa agagcagaaa tccagtctgc atggaaacag cctgtagagn 240
 agaagtttcc agtgataagt gttcactgtt ctaaggaggt acaccacagc tacctgaatt 300
 ttcccaaaat gagtgttct gtgcgttaca actggccttt gtacttgact gtgatgactt 360
 tgttttttct tttcaattct anatgaacat gggaaaaaat g 401

<210> 271

<211> 329

<212> DNA

<213> Homo sapien

<400> 271

ccacagcctc caagtcagggt ggggtggagt cccagagctg cacagggttt ggcccaagtt 60
 tctaaggag gcaacttctc ccctcgccca tcagtgccag ccctgctgg ctggtgctg 120

```

agccccctcag acagccccct gccccgcagg cctgccttct cagggacttc tgcggggcct      180
gaggcaagcc atggagtgag acccaggagc cggacacttc tcaggaaatg gcttttccca      240
acccccagcc cccaccgggt ggttcttctt gttctgtgac tgtgtatagt gccaccacag      300
cttatggcat ctcattgagg acaaaaaaa      329

```

<210> 272

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 272

```

nggctgntaa cntcggagggt nacttctctgg actatcctgg agaccccctc cgcttccacg      60
nncatnatat cnetcatngc tgggcccntn angacacnat cccactccaa cacctgngng      120
atgctggnccn cctnggaacc ancntcagaa ngaccctgnt cntntgtntt cgcgaanctg      180
aagmnaangc gggntacacc tncntgcant ggnccacnct gcngggaaact ntacacacct      240
acgggatgtg gctgcgccan gagccaagag cntttctgga tgattcccca gcctcttgnn      300
agggantcta caacattgct nnttaccttt ntccnncngc nntntntgga ntacaggngn      360
tnntaacact acatcttttt tactgcncnn tnccttggtgg g      401

```

<210> 273

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 273

```

cagcaccatg aagatcaaga tcatcgcacc cccagagcgc aagtactcgg tgtggatcgg      60
tggtccatc ctggcctcac tgtccacctt ccagcagatg tggattagca agcaggagta      120
cgaagagtcg ggcctccca tcgtccaccg caaatgcttc taaacggact cagcagatgc      180
gtagcatttg ctgcatgggt taattgagaa tagaaatttg cccctggcaa atgcacacac      240
ctcatgctag cctcacgaaa ctggaataag ccttcgaaaa gaaattgtcc ttgaagcttg      300
tatctgatat cagcactgga ttgtagaact tgttgctgat tttgaccttg tattgaagtt      360
aactgttccc cttggtatta acgtgtcagg gctgagtnt c      401

```

<210> 274

<211> 401

<212> DNA

<213> Homo sapien

<400> 274

```

ccaccacac ccaccgcgc ctcgttcgcc tcttctcgg gagccagtc gcgccaccgc      60
cgccgcccag gccatcgcca cctccgcag ccatgtccac caggtcctgt tctcgtcct      120
cctaccgcag gatgttcggc ggccggggca ccgcgagcgc gccagctcc agcggagct      180
acgtgactac gtccaccgc acctacagcc tgggcagcgc gctgcgccc agcaccagcc      240
gcagcctcta cgctcgtcc ccggggcggc tgtatgccac gcgctcctct gccgtgcgc      300
tgccgagcag cgtgcccggg gtgcggctcc tgcaggactc ggtggacttc tcgctggccg      360

```

acgccatcaa caccgagttc aagaacaccc gcaccaacga g 401

<210> 275
<211> 401
<212> DNA
<213> Homo sapien

<400> 275
ccacttccac cactttgttg agcagtgcct tcagcgcaac ccggatgcca ggtatccctg 60
ctggcctggg cctgggcttc gggagagcag aggggtgctca ggagggttaag gccaggggtg 120
gaagggaactt acctcccaaa ggttctgcag gggaatctgg agctacacac aggagggatc 180
agctcctggg tgtgtcagag gccagcctgg ggagctctgg ccactgcttc ccatgagctg 240
agggagaggg agaggggacc cgaggctgag gcataagtgg caggatttcg ggaagctggg 300
gacacggcag tgatgtgag gtctctctc ccctttccct ccaggcccag tgccagcacc 360
ctctgaacc actctttctt caagcagatc aagcgacgtg c 401

<210> 276
<211> 401
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(401)
<223> n = A,T,C or G

<400> 276
tctgatattg ntacccttga gccacctaag ttagaagaaa ttggaaatca agaagttgtc 60
attgttgaag aagcacagag ttcagaagac tttaacatgg gctcttcctc tagcagccag 120
tatactttct gtcagccaga aactgtattt tcatctcagc ctagtgtatga tgaatcaagt 180
agtgatgaaa ccagtaatca gccagtcctt gccttttagac gacgccgtgc taggaagaag 240
accgtttctg cttcagaatc tgaagaccgg ctagtgtggtg aacaagaaac tgaaccttct 300
aaggagttga gtaaactgca gttcagtagt ggtctcaata agtgtgttat acttgctttg 360
gtgattgcaa tcagcatggg atttggccat ttctatggca c 401

<210> 277
<211> 401
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(401)
<223> n = A,T,C or G

<400> 277
aactttggca acatatctca gcaaaaacta cagctatgtt attcatgcca aaataaaagc 60
tgtgcagagg agtggctgca atgaggtcac aacgggtggtg gatgtaaaag agatcttcaa 120
gtcctcatca cccatccctc gaactcaagt cccgctcatt acaaattctt cttgccagtg 180
tccacacatc ctgccccatc aagatgttct catcatgtgt tacgagnggc gctcaaggat 240
gatgcttctt gaaaattgct tagttgaaaa atggagagat cagcttagta aaagatccat 300
acagtgggaa gagaggctgc aggaacagcg ganaacagtt caggacaaga agaaaacagc 360
cgggcgcacc agtcgtagta atcccccaa accaaagggga a 401

<210> 278

<211> 401
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (401)
 <223> n = A,T,C or G

<400> 278

aatgagtgtg agaccacaaa tgaatgccgg gaggatgaaa tgtggttgaa ttatcatggc	60
ggcttcctgt gttatccacg aaatccttgt caagatccct acattctaac accagagAAC	120
cgatgtgttt gccagtcctc aaatgccatg tgccgagAAC tgccccagtc aatagtctac	180
aaatacatga gcatccgacg tgataggtct gtgccatcag acatcttcca gatacaggcc	240
acaactatit atgccaacac catcaatact ttccggatta aatctggaaa tgaaaatgga	300
gagtctacct acgacaacaa anccctgtaa gtgcaatgct tgtgctcgtg aagncattat	360
caggaccaag agaacatata gtggacctgg agatgctgac a	401

<210> 279
 <211> 401
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (401)
 <223> n = A,T,C or G

<400> 279

aaattattgc ctctgataca tacctaagtn aacanaacat taatacctaa gtaaacataa	60
cattacttgg aggggtgcag nttctaantg aaactgtatt tgaaactttt aagtatactt	120
taggaaacaa gcatgaacgg cagtctagaa taccagaaac atctacttgg gtagcttggg	180
gccattatcc tgtggaatct gatatgtctg gnagcatgtc attgatggga catgaagaca	240
tctttggaaa tgatgagatt atttcctgtg ttaaaaaaaaa aaaaaatctt aaattcctac	300
aatgtgaaac tgaaactaat aattttgatc ctgatgtatg ggacagcgta tctgtaccag	360
gctctaaata acaaaagnta gggngacaag nacatgttcc t	401

<210> 280
 <211> 326
 <212> DNA
 <213> Homo sapien

<400> 280

gaagtggAat tgtataattc aattcgataa ttgatctcat gggctttccc tggaggaaag	60
gttttttttg ttgttttttt ttaagaact tgaaacttgt aaactgagat gtctgtagct	120
tttttgccca tctgtagtgt atgtgaagat ttcaaaacct gagagcactt tttctttgtt	180
tagaattatg agaaaggcac tagatgactt taggatttgc atttttccct ttattgcctc	240
atttcttgtg acgccttggt ggggagggaa atctgtttat tttttcctac aaataaaaag	300
ctaagattct atatcgcaaa aaaaaa	326

<210> 281
 <211> 374
 <212> DNA
 <213> Homo sapien

<400> 281

caacgcgttt gcaaattatc ccctggtagc ctacttcctt acccccgaat attggttaaga	60
tgcagcaatg gcttcaggac atgggttctc ttctcctgtg atcattcaag tgctcactgc	120
atgaagactg gcttgtctca gtgtttcaac ctcaccaggg ctgtctcttg gtccacacct	180
cgctccctgt tagtgccgta tgacagcccc catcaaata ccttgGCCaa gtcacggttt	240
ctctgtggtc aagggttggt ggctgattgg tggaaagtag ggtggacca aggaggccac	300
gtgagcagtc agcaccagtt ctgcaccagc agcgccctcg tctagtggg tgttctctgtt	360
tctctggcc ctgg	374

<210> 282

<211> 404

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(404)

<223> n = A,T,C or G

<400> 282

agtgtggtgg aattcccga tctanncg cgaactcac aaggcagagt ngccatggag	60
aaaattccag tgcagcatt cttgctcctt gtggccctct cctacactct ggccagagat	120
accacagtca aacctgnagc caaaaaggac acaaaggact ctgcaccaa actgccccan	180
accctctcca gaggttgagg tgaccaactc atctggactc anacatatga agaagctcta	240
tataaatcca agacaagcaa caaaccttg atgattatc atcacttga tgagtgccca	300
cacagtcaag ctttaaagaa agtgtttgct gaaaataaag aaatccagaa attggcagag	360
cagtttgtec tctcaatct ggtttatgaa acaactgaca aaca	404

<210> 283

<211> 184

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(184)

<223> n = A,T,C or G

<400> 283

agtgtggtgg aattcacttg cttaanttgt gggcaaaaga gaaaaaga gattgatcag	60
agcattgtgc aatacagttt cattaactcc ttccctcgct ccccaaaaa tttgaatttt	120
tttttcaaca ctcttacacc tgttatggaa aatgtcaacc tttgtaagaa aacaaaaata	180
aaaa	184

<210> 284

<211> 421

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(421)

<223> n = A,T,C or G

<400> 284

```

ctattaatcc tgccacaata tttttaatta cgtacaaaga tctgacatgt caccagggga      60
cccatttcac ccactgctct gtttggccgc cagtcttttg tctctctctt cagcaatggg      120
gaggcgggata cccttcctc ggggaanana aatccatggg ttgttgccct tgccaataac      180
aaaaatggtg gaaagtcgag tggcaaagct gttgccattg gcatctttca cgtgaaccac      240
gtcaaaagat ccagggtgcc tctctctgtt ggtgatcaca ccaattcttc ctaggttagc      300
acctccagtc accatacaca ggttaccagt gtcgaacttg atgaaatcag taatcttgcc      360
agtctctaaa tcaatctgaa tggatatcatt caccttgatg aggggatcgg ggtagcggat      420
g                                                                                   421

```

<210> 285

<211> 361

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(361)

<223> n = A,T,C or G

<400> 285

```

ctgggtggtg actctttatt tcattgtccg gaanaaagat gggagtggga acagggtgga      60
cactgtgcag gcttcagctt ccactccggg caggattcag gctatctggg accgcaggga      120
ctgccagtg cagagccctg gctcccaggg caggcaggca aggtgacggg actggaagcc      180
cttttcanag ccttggagga gctggtccgt ccacaagcaa tgagtgccac tctgcagttt      240
gcaggggatg gataaacagg gaaacactgt gcattcctca cagccaacag ttaggtctt      300
ggtgaagccc cggcgctgag ctaagctcag gctgttccag ggagccacga aactgcagg      360
a                                                                                   361

```

<210> 286

<211> 336

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(336)

<223> n = A,T,C or G

<400> 286

```

tttgagtggc agcgcttta tttgtggggg ccttcaaggn agggctcgtg ggggcagcgg      60
ggaggaanag ccganaaact gtgtgaccgg ggcctcaggg ggtgggcatt gggggctcct      120
cttgcanaag ccattggca tcaccggtgc agccattggg ggcagcgggt accggtcctt      180
tcttgttcaa catagggtag gtggcagcca cgggtccaac tcgcttgagg ctgggacctg      240
ggcgctccat tttgtgttcc angagcatgt ggttctgtgg cgggagcccc acgcaggccc      300
tgaggatgtt ctgatgcag ctgcgctggc ggaaaaa                                     336

```

<210> 287

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 287

tgggtacca	atttntttat	ttgaaggaa	ggnacaaatc	aaanaactta	agnggatgtt	60
ttggtacaac	ttatanaaaa	ggnaaaggaa	accccaacat	gcattgcctg	ccttgngac	120
caggaagtc	acccacggc	tatggggaaa	ttancccgag	gcttancttt	cattatcact	180
gtctcccagg	gngngcttgt	caaaaanata	ttccnccaag	ccaaattcgg	gcgctcccat	240
nttgcncaa	gtgtcacgt	ggtcacccaa	ttctttgatg	gctttcacct	gctcattcag	300
g						301

<210> 288

<211> 358

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (358)

<223> n = A,T,C or G

<400> 288

aagtttttaa	actttttatt	tgcatattaa	aaaaattgng	cattccaata	attaaaatca	60
tttgaacaaa	aaaaaaaaatg	gcactctgat	taaactgcac	tacagcctgc	aggacacctt	120
gggacagctt	ggttttactc	tanatttcac	tgtcgtccca	ccccacttct	tccacccccac	180
ttcttccttc	accaacatgc	aagttctctc	cttccctgcc	agccanatag	atagacagat	240
gggaaaggca	ggcgggcct	tcgttgtcag	tagttctttg	atgtgaaagg	ggcagcacag	300
tcatttaaac	ttgatccaac	ctctttgcac	cttacaaggt	taaacagcta	aaagaagt	358

<210> 289

<211> 462

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (462)

<223> n = A,T,C or G

<400> 289

ggcatcagaa	atgctgttta	tttctctgct	gtccccaagc	tggctggcct	ttgcagagga	60
gcagacaaca	gatgcatagt	tgggganaaa	gggaggacag	gttccaggat	agaggggtgca	120
ggctgaggga	ggaagggtaa	naggaaggaa	ggccatcctg	gatccccaca	tttcagtctc	180
anatgaggac	aaagggactc	ccaagcccc	aatcatcan	aaaacaccaa	ggagcaggag	240
gagcttgagc	aggccccagg	gagcctcana	gccataccag	ccactgtcta	cttcccatcc	300
tcctctccca	ttccctgtct	gtttcanacc	acctccagc	taagccccag	ctccattccc	360
ccaatcctgg	cccttgccag	cttgacagtc	acagtgcctg	gaattccacc	actgaggctt	420
ctcccagttg	gattaggacg	tcgccctgtt	agcatgctgc	cc		462

<210> 290

<211> 481

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (481)

<223> n = A,T,C or G

<400> 290

tacttttcta	aacttttatta	aagaaaaaag	caataagcaa	tggnggtaaa	tctctanaac	60
atacccaatt	ttctgggctt	cctcccccga	gaatgtgaca	ttttgatttc	caaacatgcc	120
anaagtgtat	ggttcccaac	tgtactaaag	taggtganaa	gctgaagtcc	tcaagtgttc	180
atcttccaac	ttttcccagt	ctgtggctctg	tctttggatc	agcaataatt	gcctgaacag	240
ctactatggc	ttcgttgatt	tttgtctgta	gctctctgag	ctcctctatg	tgcagcaatc	300
gcanaatttg	agcagcttca	ttaanaactg	catctcctgt	gtcaaaacca	anaatatgtt	360
tgtctaaagc	aacaggtaag	ccctcttttg	tttgatttgc	cttancaact	gcacccctgtg	420
tcaggcgctc	ctgaacccaa	atccgaattg	ccttaagcat	taccaggtaa	tcacatcatgac	480
g						481

<210> 291

<211> 381

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (381)

<223> n = A,T,C or G

<400> 291

tcataagtaat	gtaaaaccat	ttgtttaatt	ctaaatcaaa	tcactttcac	aacagtgtaaa	60
attagtgact	ggttaaggng	tgccactgta	catatcatca	ttttctgact	ggggtcaggga	120
cctggctcta	gtccacaagg	gtggcaggag	gaggggtggag	gctaanaaca	cagaaaacac	180
acaaaanaaa	ggaaagctgc	cttggcanaa	ggatgaggng	gtgagcttgc	cgaaggatgg	240
tgggaagggg	gctccctgtt	ggggccgagc	caggagtccc	aagtcagctc	tcctgcctta	300
cttagctcct	ggcanagggt	gagtggggac	ctacgaggtt	caaaatcaaa	tggcatttgg	360
ccagcctggc	tttactaaca	g				381

<210> 292

<211> 371

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (371)

<223> n = A,T,C or G

<400> 292

gaaaaaataa	tcggtttaat	tgaaaaacct	gnaggatact	attccactcc	cccanatgag	60
gaggctgagg	anaccaaacc	cctacatcac	ctcgtagcca	cttctgatac	tcttcacgag	120
gcagcaggca	aagacaattc	ccaaaaacctc	nacaaaagca	attccaaggg	ctgctgcagc	180
taccaccanc	acatttttcc	tcagccagcc	cccaatcttc	tcacacacgc	cctccttatg	240
gatgccttc	tcgttgaaat	taatcccaca	gccacagta	acattaatgc	ancaggagtc	300
ggggactcgg	ttcttcgaca	tgggaaggat	tttctcccaa	tctgtgtagt	tagcagcccc	360
acagcactta	a					371

<210> 293

<211> 361

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (361)
 <223> n = A,T,C or G

<400> 293

```

gattttaaag aaaacacttt attgttcagc aattaaaagt tagccaaata tgtatttttc      60
tccataatTT attgngatgt tatcaacatc aagtaaaatg ctcatTTTca tcatttgctt      120
ctgttcatgt tttcttgaac aegtcttcaa ttttcttcc aaaatgctgc atgccacact      180
tgaggtaacg aagcanaagt atttttaaac atgacagcta anaacattca tctacagcaa      240
cctatatgct caatacatgc cgcgtgatcc tagtagtttt ttcacaacct tctacaagtt      300
tttgaaaaac atctgttatg atgactttca tacaccttca cctcaaaggc tttcttgcaC      361

```

<210> 294
 <211> 391
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (391)
 <223> n = A,T,C or G

<400> 294

```

tattttaaag tttattatg attcanaaaa aatcgagcga ataactttct ctgaaaaaat      60
atattgactc tgtatanacc acagttattg gggganaagg gctggtaggt taaattatcc      120
tattttttat tctgaaaatg atattaatan aaagtccecg ttccagtctg attataaaga      180
tacatatgcc caaaatggct ganaataaat acaacaggaa atgcaaaagc tgtaaaagcta      240
agggcatgca ananaaaatc tcanaatacc caaagnggca acaaggaacg tttggctgga      300
atttgaagtt atttcagtca tctttgtctt tggctccatg tttcaggatg cgtgtgaact      360
cgatgtaatt gaaattcccc tttttatcaa t                                     391

```

<210> 295
 <211> 343
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (343)
 <223> n = A,T,C or G

<400> 295

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ttcttttgtt ttattgataa cagaaactgt gcataattac agatttgatg aggaatctgc      60
aaataataaa gaatgtgtct actgccagca aaatacaatt attccatgcc ctctcaacat      120
acaaatatag agttcttcac accanatggc tctgggtgtaa caaagccatt ttanatgttt      180
aattgtgctt ctacaaaacc ttcanagcat gaggtagtgt cttttaccta cnatattttc      240
cacattttca ttattacact tttagtgagc taaaatcctt ttaacatagc ctgcggatga      300
tctttcacaa aagccaagcc tcatttacaa agggttttatt tct                                     343

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<210> 296
 <211> 241
 <212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(241)

<223> n = A,T,C or G

<400> 296

ttcttgata ttggttgtt ttgtgaaaaa gtttttgtt ttcttctcag tcaactgaat	60
tatttctcta ctttgccctc ctgatgccca catgananaa cttaanataa tttctaacag	120
cttcacttt ggaaaaaaa aaaacctgtt ttctcatgg aaccccagga gttgaaagt	180
gatanatgc tctcaaatc taaggctctg ttcagcttta cattatgtta cctgacgtt	240
t	241

<210> 297

<211> 391

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(391)

<223> n = A,T,C or G

<400> 297

gttgtggctg anaatgctgg agatgctcag ttctctccct cacaaggtag gccacaaatt	60
cttggtgggtg ccctcacatc tggggtcttc aggcaccagc catgctgcc gaggagtgt	120
gtcaggacan accatgtccg tgctaggccc aggcacagcc caaccactcc tcatccaagt	180
ctctcccagg ttcttggtcc cgatgggcaa ggatgacccc tccagtggct ggtacccccc	240
catcccacta ccctcacat gctctcactc tccatcaggt ccccaatcct ggcttcctc	300
ttcacgaact ctcaagaaa aggaaggata aaacctaat aaaccagaca gaagcagctc	360
tggaaaagta caaaaagaca gccagagggtg t	391

<210> 298

<211> 321

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(321)

<223> n = A,T,C or G

<400> 298

caagccaaac tgtntccagc tttattaaan atactttcca taaacaatca tggattttca	60
ggcaggacat gggcanacaa tegttaacag tatacaacaa ctttcaaact cccttnttca	120
atggactacc aaaaatcaaa aagccactat aaaacccaat gaagtcttca tctgatgtc	180
tgaacagggg aagtttaaag ngagggttga catttcacat ttagcatgtt gtttaacaac	240
ttttcacaag cggaccctga ctttcaggaa gtgaaatgaa aatggcanaa tttatctgaa	300
natccacaat ctaaaaatgg a	321

<210> 299

<211> 401

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(401)
 <223> n = A,T,C or G

<400> 299
 tatcataaag agtgttgaag tttattttatt atagcaccat tgagacattt tgaaattgga 60
 attggtaaaa aaataaaaca aaaagcattt gaattgtatt tggnggaaca gcaaaaaaag 120
 agaagtatca tttttctttg tcaaattata ctgtttccaa acatttttga aataaataac 180
 tggaaatttg tcggtcactt gcaactgggtg acaagattag aacaagagga acacatatgg 240
 agttaaatat tttttgttgg gatttcanat agagtttggg ttataaaaag caaacagggc 300
 caacgtccac accaaattct tgatcaggac caccaatgtc atagggngca atatctacaa 360
 taggtagtct cacagccttg cgtgttcgat attcaaagac t 401

<210> 300
 <211> 188
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(188)
 <223> n = A,T,C or G

<400> 300
 tgaatgcttt gtcataattaa gaaagttaaa gtgcaataat gtttgaanac aataagtggg 60
 ggtgtatctt gtttctaata agataaaactt ttttgtcttt gctttatctt attagggagt 120
 tgtatgtcag tgtataaaac atactgtgtg gtataacagg cttataaaat tctttaaaag 180
 gaaaaaaa 188

<210> 301
 <211> 291
 <212> DNA
 <213> Homo sapien

<400> 301
 aagattttgt tttattttat tatggctaga aagacactgt tatagccaaa atcggaatg 60
 aactaaaga aatcctctgt gcttttcaat atgcaaatat atttcttcca agagttgccc 120
 tgggtgact tcaagagttc atgttaactt cttttctgga aacttccttt tcttagttgt 180
 tgtattcttg aagagcctgg gccatgaaga gcttgccata gttttgggca gtgaactcct 240
 tgatgttctg gcagtaagtg tttatctggc ctgcaatgag cagcgagtc a 291

<210> 302
 <211> 341
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(341)
 <223> n = A,T,C or G

<400> 302
 tgatttttca taattttatt aatnatcac tgggaaaact aatggttcgc gtatcacaca 60


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attacactac aatctgatag gagtggtaaa accagccaat ggaatccagg taaagtacaa      120
aaacgccacc ttttattgtc ctgtcttatt tctcggaag gagggttcta ctttacacat      180
ttcatgagcc agcagtggaac ttgagttaca atgtgtaggt tccttgtggt tatagctgca      240
gaagaagcca tcaaattctt gaggacttga catctctcgg aaagaagcaa actagtggat      300
ccccggggt gcaggaattc gatatcaagc ttatcgatac c                          341

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<210> 303

<211> 361

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (361)

<223> n = A,T,C or G

<400> 303

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tgcagacagt aaatnaattt tatttgngtt cacagaacat actaggcgat ctgcacagtc      60
gctccgtgac agcccaccaa cccccaaccc tntacctcgc agccacccta aaggcgactt      120
caanaanatg gaaggatctc acggatctca ttcctaattg tccgccgaag tctcacacag      180
tanacagacg gagttganat gctggaggat gcagtcacct cctaaactta cgaccaccca      240
ccanaattca tcccagccgg gacgtcctcc cccaccggag tcctcctccat ttcttctcct      300
actttgccgc agttccaggn gtctgtcttc caccagtccc acaaagctca ataaatacca      360
a

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<210> 304

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (301)

<223> n = A,T,C or G

<400> 304

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ctctttacaa cagcctttat ttncggccct tgatcctgct cggatgctgg tggaggccct      60
tagctccgcc cgccaggctc tgtgcccgtt ccccgaggcc gcanattcat gaacacgggtg      120
ctcagggggt tgaggccgta ctccccagc gggagctggt cctccagggg cttccctcgg      180
aaggtcagcc anaacaggtc gtctgcaca ccctccagcc cgctcacttg ctgcttcagg      240
tgggccacgg tctgcgtcag ccgcacctcg taggtgctgc tgcggccctt gttattcctc      300
a

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<210> 305

<211> 331

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (331)

<223> n = A,T,C or G

<400> 305

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ganaggctag taacatcagt tttattgggt tggggnggca accatagcct ggctgggggn      60

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ggggctggcc	ctcacaggtt	gttgagttcc	agcagggtct	ggccaaggt	ctggtgaatc	120
tcgacgttct	cctccttggc	actggccaag	gtctcttcta	ggcatcgat	ggttttctcc	180
aactttgcca	canacctctc	ggcaaactct	gctcgggtct	cancctcctt	cagcttctcc	240
tccaacagtt	tgatctctc	ttcatattta	tcttcttggg	gggaatactc	ctcctctgag	300
gccatcaggg	acttgagggc	ctggtccatg	g			331

<210> 306
 <211> 457
 <212> DNA
 <213> Homo sapien

<400> 306						
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agcagtgc	aatttaaaagg	actgttttgt	tctcaaagtt	gcaagtttca	aagccaaaag	120
aattatatgt	atcaaatata	taagtaaaaa	aaagtttagac	tttcaagcct	gtaatcccag	180
cactttggga	ggctgaggca	ggtggatcac	taacattaaa	aagacaacat	tagattttgt	240
cgatttatag	caattttata	aatatataac	tttgcactt	ggatcctgaa	gcaaaaataat	300
aaagtgaatt	tgggattttt	gtacttggt	aaaagtttaa	caccctaaat	tcacaactag	360
tggatcccc	gggctgcagg	aattcgatat	caagcttata	gataccgtcg	acctcgaggg	420
ggggcccggt	acccaattcg	ccctatagtg	agtcgta			457

<210> 307
 <211> 491
 <212> DNA
 <213> Homo sapien

<400> 307						
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ccgtcacctc	ttcacgcac	cctcggactg	ccccaaaggc	cccgccgccc	ctccagccgc	120
gcgcagccac	cgccgcccgc	gccgcctctc	cttagtcgcc	gccatgacga	ccgcgtccac	180
ctcgcaggtg	cgccagaact	accaccagga	ctcagaggcc	gccatcaacc	gccagatcaa	240
cctggagctc	tacgcctcct	acgtttacct	gtccatgtct	tactactttg	accgcgatga	300
tgtggctttg	aagaactttg	ccaaataactt	tcttaccaca	tctcatgagg	agagggaaca	360
tgctgagaaa	ctgatgaagc	tgacagaacca	acgaggtggc	cgaatcttcc	ttcaggatat	420
caagaaacca	gactgtgatg	actgggagag	cggtctgaat	gcaatggagt	gtgcattaca	480
tttgaaaaa	a					491

<210> 308
 <211> 421
 <212> DNA
 <213> Homo sapien

<400> 308						
ctcagcgtt	cttctttctt	ggtttgatcc	tgactgctgt	catggcgtgc	cctctggaga	60
aggccctgga	tgtgatggtg	tcaccttcc	acaagtactc	gggcaaagag	ggtgacaagt	120
tcaagctcaa	caagtcagaa	ctaaaggagc	tgctgaccog	ggagctgccc	agcttcttgg	180
ggaaaaggac	agatgaagct	gctttccaga	agctgatgag	caacttggac	agcaacaggg	240
acaacyaggt	ggacttccaa	gagtactgtg	tcttctgtgc	ctgcatcgcc	atgatgtgta	300
acgaattctt	tgaaggttc	ccagataagc	agcccaggaa	gaaatgaaaa	ctcctctgat	360
gtggttgggg	ggtctgccag	ctggggccct	ccctgtcgcc	agtgggcact	tttttttttc	420
c						421

<210> 309
 <211> 321
 <212> DNA

<213> Homo sapien

<400> 309

accaaattggc	ggatgacgcc	ggtgcagcgg	gggggcccgg	gggccctggg	ggccctggga	60
tggggaaccg	cgttggttc	cgcggaggtt	tcggcagtg	catccggggc	cggggtcgcg	120
gccgtggacg	gggcccgggc	caggcccgcg	gagctcgcg	aggcaaggcc	gaggataagg	180
agtggatgcc	cgtcaccaag	ttgggcccgt	tggtcaagga	catgaagatc	aagtcctgg	240
aggagatcta	tctcttctcc	ctgccatta	aggaatcaga	gatcattgat	ttcttcctgg	300
gggcctctct	caaggatgag	g				321

<210> 310

<211> 381

<212> DNA

<213> Homo sapien

<400> 310

ttaaccagcc	atattggctc	aataaatagc	ttcggtaagg	agttaatttc	cttctagaaa	60
tcagtgccta	tttttctgg	aaactcaatt	ttaaatagtc	caattccatc	tgaagccaag	120
ctgttgcat	tttcattcgg	tgacattctc	tcccatgaca	cccagaaggg	gcagaagaac	180
cacatttttc	atttatagat	gtttgcatcc	tttgtattaa	aattattttg	aaggggttgc	240
ctcattggat	ggcttttttt	tttttctctc	agggagaagg	ggagaaatgt	acttggaaat	300
taatgtatgt	ttacatctct	ttgcaaattc	ctgtacatag	agatatattt	tttaagtgtg	360
aatgtaacaa	catactgtga	a				381

<210> 311

<211> 538

<212> DNA

<213> Homo sapien

<400> 311

tttgaattta	caccaagaac	ttctcaataa	aagaaaatca	tgaatgctcc	acaattttcaa	60
cataccacaa	gagaagttaa	tttcttaaca	ttgtgttcta	tgattatttg	taagaccttc	120
accaagtctc	gatatctttt	aaagacatag	ttcaaaattg	cttttgaaaa	tctgtattct	180
tgaaaatatc	cttgttgtgt	attaggtttt	taaataaccag	ctaaaggatt	acctcactga	240
gtcatcagta	ccctcctatt	cagctcccca	agatgatgtg	tttttgctta	ccctaagaga	300
ggttttcttc	ttatttttag	ataattcaag	tgcttagata	aattatgttt	tctttaagtg	360
tttatggtaa	actcttttaa	agaaaattta	atatgttata	gctgaatctt	tttggttaact	420
ttaaatcttt	atcatagact	ctgtacatat	gttcaaatta	gctgcttgcc	tgatgtgtgt	480
atcatcggtg	ggatgacaga	acaaacatat	ttatgatcat	gaataatgtg	ctttgtaa	538

<210> 312

<211> 176

<212> DNA

<213> Homo sapien

<400> 312

ggaggagcag	ctgagagata	gggtcagtga	atgcggttca	gcctgctacc	tctcctgtct	60
tcatagaacc	attgccttag	aattattgta	tgacacgttt	tttgttggtt	aagctgtaag	120
gttttgttct	ttgtgaacat	gggtattttg	aggggagggg	ggaggagta	gggaag	176

<210> 313

<211> 396

<212> DNA

<213> Homo sapien

<400> 313

ccagcacc	ccc caggccctg	gggacctggg	ttctcagact	gccaaagaag	ccttgccatc	60
tggegtccc	atggctcttg	caacatctcc	ccttcgtttt	tgaggggggc	atgccggggg	120
agccaccagc	ccctcactgg	gttcggagga	gagtcaggaa	gggccaaagca	cgacaaagca	180
gaaacatcgg	atttggggaa	cgcggtgcaa	tcccttggtc	cgcagggctg	ggcgggagag	240
actgttctgt	tccttggtga	actgtgttgc	tgaaagacta	cctcgttctt	gtcttgatgt	300
gtcacggggg	caactgcctg	ggggcgggga	tgggggcagg	gtggaagcgg	ctccccattt	360
tataccaaag	gtgctacatc	tatgtgatgg	gtgggg			396

<210> 314

<211> 311

<212> DNA

<213> Homo sapien

<400> 314

cctcaacatc	ctcagagagg	actggaagcc	agtccttacg	ataaactcca	taatttatgg	60
cctgcagtat	ctcttcttgg	agcccaaccc	cgaggacca	ctgaacaagg	aggccgcaga	120
ggctctgcag	aacaaccggc	ggctgtttga	gcagaacgtg	cagcgctcca	tgccgggtgg	180
ctacatcggc	tccacctact	ttgagcgctg	cctgaaatag	ggttggcgca	taccaccccc	240
cgccacggcc	acaagccctg	gcatccccctg	caaatatatta	ttggggggcca	tgggtagggg	300
tttggggggc	g					311

<210> 315

<211> 336

<212> DNA

<213> Homo sapien

<400> 315

ttttagaacat	ggttatcatc	caagactact	ctaccctgca	acattgaact	cccaagagca	60
aatccacatt	cctcttgagt	tctgcagctt	ctgtgtaaat	agggcagctg	tcgtctatgc	120
cgtagaatca	catgatctga	ggaccattca	tggaaagctg	taaatagcct	agtctggggg	180
gtcttccata	aagttttgca	tggagcaaac	aaacaggatt	aaactaggtt	tggttecttc	240
agccctctaa	aagcataggg	cttagcctgc	aggcttcctt	gggctttctc	tgtgtgtgta	300
gttttgtaaa	cactatagca	tctgttaaga	tccagt			336

<210> 316

<211> 436

<212> DNA

<213> Homo sapien

<400> 316

aacatgggtct	gcgtgcctta	agagagacgc	ttcctgcaga	acaggacctg	actacaaaga	60
atgtttccat	tggattgtt	ggtaaagact	tggagtttac	aatctatgat	gatgatgatg	120
tgtctccatt	cctggaaggt	cttgaagaaa	gaccacagag	aaaggcacag	cctgctcaac	180
ctgctgatga	acctgcagaa	aaggctgatg	aaccaatgga	acattaagtg	ataagccagt	240
ctatatatgt	attatcaaatt	atgtaagaat	acaggcacca	catactgatg	acaataatct	300
atactttgaa	ccaaaagttg	cagagtgggtg	gaatgctatg	tttttaggaat	cagtccagat	360
gtgagttttt	tccaagcaac	ctcactgaaa	cctatataat	ggaatacatt	tttctttgaa	420
aggggtctgta	taatca					436

<210> 317

<211> 196

<212> DNA

<213> Homo sapien

<400> 317

tattccttgt gaagatgata tactatTTTT gttaagcgtg tctgtattta tgtgtgagga	60
gctgctggct tgcagtgcgc gtgcacgtgg agagctgggt cccggagatt ggacggcctg	120
atgctccctc ccctgccctg gtccagggaa gctggccgag ggtcctggct cctgaggggc	180
atctgccctt ccccca	196

<210> 318

<211> 381

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(381)

<223> n = A,T,C or G

<400> 318

gacgcttng ccgtaacgat gatcggagac atcctgctgt tccggacgtt gctgatgaat	60
gccggggcgg tgctgaactt taagctgaaa aagaaggaca cncagggcct tggggaggag	120
tncagggagc ccaacacagg tgacaacatc cgggaattct tgctgancct cagatacttt	180
cnaatcttca tcnccctgtg gaacatcttc atgatgttct gcatgattgt gctgntcggc	240
tcttgaatcc cancgatgaa accannaact cactttcccg ggatgccgan tctccattcc	300
tccattcctg atgacttcaa naatgttttt gaccaaaaaa ccgacaacct tcccagaaag	360
tccaagctcg tgggtggngg a	381

<210> 319

<211> 506

<212> DNA

<213> Homo sapien

<400> 319

ctaagcttta cgaatggggg gacaacttat gataaaaact agagctagtg aattagccta	60
tttgtaaata cttttgttat aattgatagg atacatcttg gacatggaat tgtaagcca	120
cctctgagca gtgtatgtca ggacttgctt attagggttg cagcagaggg gcagaaggaa	180
ttatacaggt agagatgtat gcagatgtgt ccatatatgt ccataattac attttgatag	240
ccattgatgt atgcatctct tggctgtact ataagaacac attaatcaa tggaaatata	300
ctttgctaatt attttaattg tatagatctg ctaatgaatt ctcttaaaaa catactgtat	360
tctgttctg tgtgtttcat tttaaattga gcattaaggg aatgcagcat ttaaatcaga	420
actctgccaa tgcttttata tagaggcgtg ttgccatttt tgtcttatat gaaatttctg	480
tccaagaaa ggcaggatta catctt	506

<210> 320

<211> 351

<212> DNA

<213> Homo sapien

<400> 320

ctgacctgca ggacgaaacc atgaagagcc tgatccttct tgccatcctg gccgccttag	60
ccgtagtaac tttgtgttat gaatcacatg aaagcatgga atcttatgaa cttaatccct	120
tcatcaacag gagaaatgca aataccttca tatcccttca gcagagatgg agagctaaag	180
tccaagagag gatccgagaa cgctctaagc ctgtccacga gctcaatagg gaagcctgtg	240
atgactacag acttttgcga cgctacgcca tggtttatgg atacaatgct gcctataatc	300
gctacttcag gaagcgccga gggaccaaat gagactgagg gaagaaaaa a	351

<210> 321

<211> 421
 <212> DNA
 <213> Homo sapien

<400> 321

ctcggaggcg	ttcagctgct	tcaagatgaa	gctgaacatc	tccttcccag	ccactggctg	60
ccagaaactc	attgaagtgg	acgatgaacg	caaacttcgt	actttctatg	agaagcgtat	120
ggccacagaa	gttgctgctg	acgctctggg	tgaagaatgg	aagggttatg	tggtccgaat	180
cagtgggtggg	aacgacaaac	aagggttccc	catgaagcag	ggtgtcttga	cccatggccg	240
tgtecgctcg	ctactgagta	aggggcattc	ctgttacaga	ccaaggagaa	ctggagaaaag	300
aaagagaaaa	tcagttcgtg	gttgcatgtg	ggatgcaa	ctgagcgttc	tcaacttggg	360
tattgtaaaa	aaaggagaga	aggatattcc	tggactgact	gatactacag	tgccctcgccg	420
c						421

<210> 322
 <211> 521
 <212> DNA
 <213> Homo sapien

<400> 322

agcagctctc	ctgccacagc	tcctcaccac	ctgaaaatgt	tcgcctgctc	caagtttgtc	60
tccactccct	ccttggtcaa	gagcacctca	cagctgctga	gccgtccgct	atctgcagtg	120
gtgctgaaac	gaccggagat	actgacagat	gagagcctca	gcagcttggc	agtctcatgt	180
ccccttacct	cacttgtctc	tagccgcagc	ttccaaacca	gcgccatttc	aaggacatc	240
gacacagcag	ccaagttcat	tggagctggg	gctgccacag	ttgggggtggc	tggttctggg	300
gctgggattg	gaactgtgtt	tgggagcctc	atcattgggt	atgccaggaa	cccttctctg	360
aagcaacagc	tcttctccta	cgccattctg	ggctttgccc	tctcggaggc	catggggctc	420
ttttgtctga	tggtagcctt	tctcatcctc	tttgccatgt	gaaggagccg	tctccacctc	480
ccatagttct	cccgcgtctg	gttggtcccg	tgtgttcctt	t		521

<210> 323
 <211> 435
 <212> DNA
 <213> Homo sapien

<400> 323

ccgaggctgc	acgcgtgaga	cttctccgcc	gcagacggcg	ccgcgatgcg	ctacgtcgcc	60
tctacactgc	tggtgcccct	agggggcaac	tcctccccca	gcgccaagga	catcaagaag	120
atcttgga	gcgtgggtat	cgaggcggac	gacgaccggc	tcaacaaggt	tatcagtga	180
ctgaatggaa	aaaacattga	agacgtcatt	gcccagggta	ttggcaagct	tgccagtgt	240
cctgctgggtg	gggctgtagc	ogtctctgct	gccccaggct	ctgcagcccc	tgctgctggg	300
tctgcccctg	ctgcagcaga	ggagaagaaa	gatgagaaga	aggaggagtc	tgaagagtca	360
gatgatgaca	tgggatttgg	cctttttgat	taaattcctg	ctcccctgca	aataaagcct	420
ttttacacat	ctcaa					435

<210> 324
 <211> 521
 <212> DNA
 <213> Homo sapien

<400> 324

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aacccagcc	tcagcctcag	ccgcaacccc	agccccaate	acaacccag	cctcagcccc	240

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aaccceaagcc tcagccccag cagctccacc cgtatccgca tccacatcca catccacact    300
ctcctectca ctgcaccca caccctcacc cgcacccgca tccgcaccaa ataccgcacc    360
cacacccaca gccgcactcg cagccgcacg ggcacccggt tctccgcagc acctccaact    420
ctgctgaaa ggggcagctc ccgggcaaga caaggttttg aggacttgag gaagtgggac    480
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<210> 325

<211> 451

<212> DNA

<213> Homo sapien

<400> 325

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tatttttact tagattactt tgggaatgag agattgttgt cttgaactct ggcactgtac    180
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acccccaccc ccaccaaga cattttaata gtaaatagag agagagagaa gagttaatga    360
acatgaggtg gtgttcact ggcaggatga cttttcaata gctcaaatca atttcagtgc    420
ctttatcact tgaattatta acttaatttg a                    451

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<210> 326

<211> 421

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(421)

<223> n = A,T,C or G

<400> 326

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ggataccgga aaaacacccg tggagccgga ggtggcaatt caccgaattc gaatcaccct    180
aacaagccgc aacgtaaaat ccttggaaaa ggtgtgtgct gacttgataa gaggcgaaa    240
agaaaagaat ctcaaagtga aaggaccagt tcgaatgcct accaagactt tgagantcac    300
tacaagaaaa actccttggt gtgaagggtc taagacgtgg gatcgtttcc agatgagaat    360
tcacaagcga ctattgact tgcacagtcc ttctgagatt gttaagcaga ttacttccat    420
c

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<210> 327

<211> 456

<212> DNA

<213> Homo sapien

<400> 327

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atccgggggc aaggccaaaa agaagaagtg gtccaaaggc aaagttcggg acaagctcaa    180
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ggcagccctt caggagctcc ttagtaaaagg acttatcaaa ctggtttcaa agcacagagc    360
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<210> 328
 <211> 471
 <212> DNA
 <213> Homo sapien

<400> 328
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 tgattatccg aaatgtttca ttgtgggagc agacaatgtg ggctccaagc agatgcagca 180
 gatccgcatg tcccttcgcg ggaaggctgt ggtgctgatg ggcaagaaca ccatgatgcg 240
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 ccgggggaat gtgggctttg tgttcaccaa ggaggacctc actgagatca gggacatggt 360
 gctggccaat aaggtgccag ctgctgcccg tgctggtgcc attgccccat gtgaagtcac 420
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<210> 329
 <211> 278
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (278)
 <223> n = A,T,C or G

<400> 329
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 ccttgatatt tttctttttt tttttttttt ttgnnggatg ggacttgatg atttttctaa 180
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<210> 330
 <211> 338
 <212> DNA
 <213> Homo sapien

<400> 330
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 cattacaatc tccagcattc cccctcaaac ctaaaaaa 338

<210> 331
 <211> 2820
 <212> DNA
 <213> Homo sapiens

<400> 331
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gctcctgaac agcatggacc agcagattcg gaacggctcc tegtccacca gtccctataa 180
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<210> 332

<211> 2270

<212> DNA

<213> Homo sapiens

<400> 332

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aaagaaagtt attaccgatc caccatgtcc cagagcacac agacaaatga attcctcagt 180
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<210> 333

<211> 2816

<212> DNA

<213> Homo sapiens

<400> 333

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aaagaaagtt attaccgatc caccatgtcc cagagcacac agacaaatga attcctcagt 180
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ccaggcccgc acagtttcga cgtgtccttc cagcagtcga gcaccgcca gtctggccacc 600
tggacgtatt ccactgaact gaagaaactc tactgccaaa ttgcaaagac atgccccatc 660

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<210> 334

<211> 2082

<212> DNA

<213> Homo sapiens

<400> 334

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<210> 335

<211> 4849

<212> DNA

<213> Homo sapiens

<400> 335

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<210> 336

<211> 1386

<212> DNA

<213> Homo sapiens

<400> 336

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aacacagacc acgcgcagaa cagcgtcagc gcgccctcgc cctacgcaca gccagctcc 180
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gagcacgtca cggaggtggt gaagcgggtg cccaaccatg agctgagcgg tgaattcaac 480
gagggacaga ttgcccctcc tagtcatttg attcgagtag aggggaacag ccatgcccag 540
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<210> 337

<211> 1551

<212> DNA

<213> Homo sapiens

<400> 337

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gtggtgaagc ggtgccccaa ccatgagctg agccgtgaat tcaacgagg acagattgcc 660
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<210> 338

<211> 586

<212> PRT

<213> Homo sapiens

<400> 338

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      20                                25                        30

Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser
      35                                40                        45

Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Pro Thr Phe Asp Ala
      50                                55                        60

Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro
      65                                70                        75                        80

His Ser Ser Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala
      85                                90                        95

Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala
      100                               105                        110

Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly
      115                               120                        125

Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr
      130                               135                        140

Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn
      145                               150                        155                        160

Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn
      165                               170                        175

Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val

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195	200	205
Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg		
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Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val		
225	230	235
Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg		
245	250	255
Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp		
260	265	270
Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr		
275	280	285
His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp		
290	295	300
Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu		
305	310	315
Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His		
325	330	335
Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu		
340	345	350
Leu Gln Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser		
355	360	365
Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val		
370	375	380
Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr		
385	390	395
Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met		
405	410	415
Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro		
420	425	430
Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro Pro		
435	440	445
Tyr Pro Thr Asp Cys Ser Ile Val Ser Phe Leu Ala Arg Leu Gly Cys		
450	455	460
Ser Ser Cys Leu Asp Tyr Phe Thr Thr Gln Gly Leu Thr Thr Ile Tyr		
465	470	475
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Gln Ile Glu His Tyr Ser Met Asp Asp Leu Ala Ser Leu Lys Ile Pro
 485 490 495
 Glu Gln Phe Arg His Ala Ile Trp Lys Gly Ile Leu Asp His Arg Gln
 500 505 510
 Leu His Glu Phe Ser Ser Pro Ser His Leu Leu Arg Thr Pro Ser Ser
 515 520 525
 Ala Ser Thr Val Ser Val Gly Ser Ser Glu Thr Arg Gly Glu Arg Val
 530 535 540
 Ile Asp Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro
 545 550 555 560
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 Lys Gln Gln Arg Ile Lys Glu Glu Gly Glu
 580 585
 <210> 339
 <211> 641
 <212> PRT
 <213> Homo sapiens
 <400> 339
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 Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
 35 40 45
 Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
 50 55 60
 Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
 65 70 75 80
 Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn
 85 90 95
 Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
 100 105 110
 Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
 115 120 125
 Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln
 130 135 140

Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys
 145 150 155 160
 Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val
 165 170 175
 Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr
 180 185 190
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His
 195 200 205
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His
 210 215 220
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro
 225 230 235 240
 Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val
 245 250 255
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser
 260 265 270
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu
 275 280 285
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg
 290 295 300
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile
 305 310 315 320
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys
 325 330 335
 Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys
 340 345 350
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly
 355 360 365
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu
 370 375 380
 Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln
 385 390 395 400
 Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser
 405 410 415
 Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser
 420 425 430
 Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg

155

435 440 445
 Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile
 450 455 460
 Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu
 465 470 475 480
 Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser
 485 490 495
 His Cys Thr Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Gly
 500 505 510
 Phe Leu Ala Arg Leu Gly Cys Ser Ser Cys Leu Asp Tyr Phe Thr Thr
 515 520 525
 Gln Gly Leu Thr Thr Ile Tyr Gln Ile Glu His Tyr Ser Met Asp Asp
 530 535 540
 Leu Ala Ser Leu Lys Ile Pro Glu Gln Phe Arg His Ala Ile Trp Lys
 545 550 555 560
 Gly Ile Leu Asp His Arg Gln Leu His Glu Phe Ser Ser Pro Ser His
 565 570 575
 Leu Leu Arg Thr Pro Ser Ser Ala Ser Thr Val Ser Val Gly Ser Ser
 580 585 590
 Glu Thr Arg Gly Glu Arg Val Ile Asp Ala Val Arg Phe Thr Leu Arg
 595 600 605
 Gln Thr Ile Ser Phe Pro Pro Arg Asp Glu Trp Asn Asp Phe Asn Phe
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 Asp Met Asp Ala Arg Arg Asn Lys Gln Gln Arg Ile Lys Glu Glu Gly
 625 630 635 640
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<210> 340

<211> 448

<212> PRT

<213> Homo sapiens

<400> 340

Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
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Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
 20 25 30

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
 35 40 45

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
 50 55 60

Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
 65 70 75 80

Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn
 85 90 95

Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
 100 105 110

Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
 115 120 125

Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln
 130 135 140

Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys
 145 150 155 160

Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val
 165 170 175

Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr
 180 185 190

Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His
 195 200 205

Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His
 210 215 220

Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro
 225 230 235 240

Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val
 245 250 255

Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser
 260 265 270

Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu
 275 280 285

Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg
 290 295 300

Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile
 305 310 315 320

Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys
 325 330 335

Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys
340 345 350

Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly
355 360 365

Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu
370 375 380

Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln
385 390 395 400

Gln Gln Gln His Gln His Leu Leu Gln Lys His Leu Leu Ser Ala Cys
405 410 415

Phe Arg Asn Glu Leu Val Glu Pro Arg Arg Glu Thr Pro Lys Gln Ser
420 425 430

Asp Val Phe Phe Arg His Ser Lys Pro Pro Asn Arg Ser Val Tyr Pro
435 440 445

<210> 341

<211> 356

<212> PRT

<213> Homo sapiens

<400> 341

Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln
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Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn
20 25 30

Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser
35 40 45

Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala
50 55 60

Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro
65 70 75 80

His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala
85 90 95

Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala
100 105 110

Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly
115 120 125

Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr
130 135 140

Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn

145 150 155 160
 Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn
 165 170 175
 Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val
 180 185 190
 Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val
 195 200 205
 Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg
 210 215 220
 Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val
 225 230 235 240
 Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg
 245 250 255
 Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp
 260 265 270
 Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Ser Arg Gln Asn Thr
 275 280 285
 His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp
 290 295 300
 Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu
 305 310 315 320
 Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His
 325 330 335
 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu
 340 345 350
 Leu Gln Lys Gln
 355
 <210> 342
 <211> 680
 <212> PRT
 <213> Homo sapiens
 <400> 342
 Met Asn Phe Glu Thr Ser Arg Cys Ala Thr Leu Gln Tyr Cys Pro Asp
 5 10 15
 Pro Tyr Ile Gln Arg Phe Val Glu Thr Pro Ala His Phe Ser Trp Lys
 20 25 30
 Glu Ser Tyr Tyr Arg Ser Thr Met Ser Gln Ser Thr Gln Thr Asn Glu
 35 40 45

Phe Leu Ser Pro Glu Val Phe Gln His Ile Trp Asp Phe Leu Glu Gln
 50 55 60

Pro Ile Cys Ser Val Gln Pro Ile Asp Leu Asn Phe Val Asp Glu Pro
 65 70 75 80

Ser Glu Asp Gly Ala Thr Asn Lys Ile Glu Ile Ser Met Asp Cys Ile
 85 90 95

Arg Met Gln Asp Ser Asp Leu Ser Asp Pro Met Trp Pro Gln Tyr Thr
 100 105 110

Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn Gly Ser
 115 120 125

Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser Val Thr
 130 135 140

Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala Leu Ser
 145 150 155 160

Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro His Ser
 165 170 175

Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala Thr Trp
 180 185 190

Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala Lys Thr
 195 200 205

Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly Ala Val
 210 215 220

Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr Glu Val
 225 230 235 240

Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn Glu Gly
 245 250 255

Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn Ser His
 260 265 270

Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val Leu Val
 275 280 285

Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val Leu Tyr
 290 295 300

Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg Arg Pro
 305 310 315 320

Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val Leu Gly
 325 330 335

Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg Asp Arg
 340 345 350
 Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp Ser Thr
 355 360 365
 Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr His Gly
 370 375 380
 Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp Glu Leu
 385 390 395 400
 Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu Leu Lys
 405 410 415
 Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His Thr Ile
 420 425 430
 Glu Thr Tyr Arg Gln Gln Gln Gln Gln Gln His Gln His Leu Leu Gln
 435 440 445
 Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser Ser Pro
 450 455 460
 Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val Ser Gln
 465 470 475 480
 Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr Ile Pro
 485 490 495
 Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met Pro Met
 500 505 510
 Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro Pro Pro
 515 520 525
 Leu Ser Met Pro Ser Thr Ser Gln Cys Thr Pro Pro Pro Pro Tyr Pro
 530 535 540
 Thr Asp Cys Ser Ile Val Ser Phe Leu Ala Arg Leu Gly Cys Ser Ser
 545 550 555 560
 Cys Leu Asp Tyr Phe Thr Thr Gln Gly Leu Thr Thr Ile Tyr Gln Ile
 565 570 575
 Glu His Tyr Ser Met Asp Asp Leu Ala Ser Leu Lys Ile Pro Glu Gln
 580 585 590
 Phe Arg His Ala Ile Trp Lys Gly Ile Leu Asp His Arg Gln Leu His
 595 600 605
 Glu Phe Ser Ser Pro Ser His Leu Leu Arg Thr Pro Ser Ser Ala Ser
 610 615 620
 Thr Val Ser Val Gly Ser Ser Glu Thr Arg Gly Glu Arg Val Ile Asp

625 630 635 640
 Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro Arg Asp
 645 650 655
 Glu Trp Asn Asp Phe Asn Phe Asp Met Asp Ala Arg Arg Asn Lys Gln
 660 665 670
 Gln Arg Ile Lys Glu Glu Gly Glu
 675 680

 <210> 343
 <211> 461
 <212> PRT
 <213> Homo sapiens

 <400> 343
 Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln
 5 10 15
 Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn
 20 25 30
 Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser
 35 40 45
 Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala
 50 55 60
 Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro
 65 70 75 80
 His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala
 85 90 95
 Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala
 100 105 110
 Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly
 115 120 125
 Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr
 130 135 140
 Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn
 145 150 155 160
 Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn
 165 170 175
 Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val
 180 185 190
 Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val
 195 200 205

Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg
 210 215 220
 Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val
 225 230 235 240
 Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg
 245 250 255
 Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp
 260 265 270
 Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr
 275 280 285
 His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp
 290 295 300
 Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu
 305 310 315 320
 Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His
 325 330 335
 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu
 340 345 350
 Leu Gln Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser
 355 360 365
 Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val
 370 375 380
 Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr
 385 390 395 400
 Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met
 405 410 415
 Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro
 420 425 430
 Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro Pro
 435 440 445
 Tyr Pro Thr Asp Cys Ser Ile Val Arg Ile Trp Gln Val
 450 455 460

<210> 344

<211> 516

<212> PRT

<213> Homo sapiens

<400> 344

Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
 5 10 15
 Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
 20 25 30
 Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
 35 40 45
 Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
 50 55 60
 Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
 65 70 75 80
 Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn
 85 90 95
 Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
 100 105 110
 Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
 115 120 125
 Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln
 130 135 140
 Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys
 145 150 155 160
 Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val
 165 170 175
 Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr
 180 185 190
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His
 195 200 205
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His
 210 215 220
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro
 225 230 235 240
 Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val
 245 250 255
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser
 260 265 270
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu
 275 280 285
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg

290 295 300
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile
 305 310 315 320
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys
 325 330 335
 Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys
 340 345 350
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly
 355 360 365
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu
 370 375 380
 Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln
 385 390 395 400
 Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser
 405 410 415
 Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser
 420 425 430
 Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg
 435 440 445
 Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile
 450 455 460
 Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu
 465 470 475 480
 Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser
 485 490 495
 His Cys Thr Pro Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Arg
 500 505 510
 Ile Trp Gln Val
 515

<210> 345

<211> 1800

<212> DNA

<213> Homo sapiens

<400> 345

gcgcctcatt gccactgcag tgactaaagc tgggaagacg ctggtcagtt cacctgcccc 60
 actggttggtt ttttaacaa attctgatac aggcgacatc ctactgacc gagcaaagat 120
 tgacattcgt atcatcactg tgcaccattg gcttctaggc actccagtgg ggtaggagaa 180

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ggaggtctga aaccctcgca gagggatctt gccctcattc tttgggtctg aaacactggc 240
agtcgttgga aacaggactc agggataaac cagcgcaatg gattggggga cgctgcacac 300
tttcatcggg ggtgtcaaca aacactccac cagcatcggg aagggtgtgga tcacagtcac 360
ctttattttc cgagtcacga tcttagtggt ggctgcccag gaagtgtggg gtgacgagca 420
agaggacttc gtctgcaaca cactgcaacc gggatgcaaa aatgtgtgct atgaccactt 480
tttcccgggtg tcccacatcc ggctgtgggc cctccagctg atcttctgtc ccaccccgagc 540
gctgctgggtg gccatgcatg tggcctacta caggcacgaa accactcgca agttcaggcg 600
aggagagaag aggaatgatt tcaaagacat agaggacatt aaaaagcaca aggttcggat 660
agaggggtcg ctgtggtgga cgtacaccag cagcatcttt ttccgaatca tctttgaagc 720
agcctttatg tatgtgtttt acttccttta caatgggtac cacctgccct ggggtgtgaa 780
atgtgggatt gacccctgcc ccaaccttgt tgactgcttt atttctaggc caacagagaa 840
gaccgtgttt accattttta tgatttctgc gtctgtgatt tgcagtctgc ttaacgtggc 900
agagttgtgc tacctgtctg tgaaagtgtg ttttaggaga tcaaagagag cacagacgca 960
aaaaaatcac cccaatcatg ccctaaagga gagtaagcag aatgaaatga atgagctgat 1020
ttcagatagt ggtcaaaatg caatcacagg tttcccaagc taaacatttc aaggtaaaat 1080
gtagctgcgt cataaggaga cttctgtctt ctccagaagg caataccaac ctgaaagttc 1140
cttctgtagc ctgaagagtt tgtaaatgac tttcataata aatagacact tgagttaact 1200
ttttgtagga tacttgctcc attcatacac aacgtaatca aatatgtggt ccatctctga 1260
aaacaagaga ctgcttgaca aaggagcatt gcagtcactt tgacaggttc cttttaagtg 1320
gactctctga caaagtgggt actttctgaa aatttatata actgttggtg ataaggaaca 1380
tttatccagg aattgatacg tttattagga aaagatatat ttataggctt ggatgttttt 1440
agttccgact ttgaatttat ataaagtatt tttataatga ctggctcttc ttacctggaa 1500
aaacatgcga tgtagttttt agaattacac cacaagtatc taaatttcca acttacaag 1560
ggcctatct tgtaaatatt gttttgcatt gtctgttggc aaatttgatg actgtcatga 1620
tacgcttaag gtgggaaagt gttcattgca caatatattt ttactgcttt ctgaatgtag 1680
acggaacagt gtggaagcag aaggcttttt taactcatcc gtttgccga tcgttgacaga 1740
ccactgggag atgtggatgt ggttgctccc ttttgcctgt ccccggtggt taacccttct 1800

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<210> 346

<211> 261

<212> PRT

<213> Homo sapiens

<400> 346

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Met Asp Trp Gly Thr Leu His Thr Phe Ile Gly Gly Val Asn Lys His
          5                      10                      15

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Ser Thr Ser Ile Gly Lys Val Trp Ile Thr Val Ile Phe Ile Phe Arg
          20                      25                      30

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Val Met Ile Leu Val Val Ala Ala Gln Glu Val Trp Gly Asp Glu Gln
          35                      40                      45

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Glu Asp Phe Val Cys Asn Thr Leu Gln Pro Gly Cys Lys Asn Val Cys
          50                      55                      60

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Tyr Asp His Phe Phe Pro Val Ser His Ile Arg Leu Trp Ala Leu Gln
          65                      70                      75                      80

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Leu Ile Phe Val Ser Thr Pro Ala Leu Leu Val Ala Met His Val Ala
          85                      90                      95

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Tyr Tyr Arg His Glu Thr Thr Arg Lys Phe Arg Arg Gly Glu Lys Arg
          100                      105                      110

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Asn Asp Phe Lys Asp Ile Glu Asp Ile Lys Lys His Lys Val Arg Ile
 115 120 125
 Glu Gly Ser Leu Trp Trp Thr Tyr Thr Ser Ser Ile Phe Phe Arg Ile
 130 135 140
 Ile Phe Glu Ala Ala Phe Met Tyr Val Phe Tyr Phe Leu Tyr Asn Gly
 145 150 155 160
 Tyr His Leu Pro Trp Val Leu Lys Cys Gly Ile Asp Pro Cys Pro Asn
 165 170 175
 Leu Val Asp Cys Phe Ile Ser Arg Pro Thr Glu Lys Thr Val Phe Thr
 180 185 190
 Ile Phe Met Ile Ser Ala Ser Val Ile Cys Met Leu Leu Asn Val Ala
 195 200 205
 Glu Leu Cys Tyr Leu Leu Leu Lys Val Cys Phe Arg Arg Ser Lys Arg
 210 215 220
 Ala Gln Thr Gln Lys Asn His Pro Asn His Ala Leu Lys Glu Ser Lys
 225 230 235 240
 Gln Asn Glu Met Asn Glu Leu Ile Ser Asp Ser Gly Gln Asn Ala Ile
 245 250 255
 Thr Gly Phe Pro Ser
 260

<210> 347

<211> 1740

<212> DNA

<213> Homo sapiens

<400> 347

atgaacaaac tgtatatcgg aaacctcagc gagaacgccg cccctcggga cctagaaagt 60
 atcttcaagg acgccaagat cccggtgtcg ggacccttcc tggatgaagac tggctacgcg 120
 ttcgtggact gcccgacga gagctgggcc ctcaaggcca tcgaggcgct ttcaggtaaa 180
 atagaactgc acgggaaacc catagaagtt gagcactcgg tcccaaaaag gcaaaggatt 240
 cggaaacttc agatacgaat tatccgcct catttacagt gggaggtgct ggatagttta 300
 ctagtccagt atggagtggg ggagagctgt gagcaagtga aactgactc ggaaactgca 360
 gttgtaaatg taacctattc cagtaaggac caagctagac aagcactaga caaactgaat 420
 ggatttcagt tagagaattt caccttgaat gtagcctata tccctgatga aacggccgcc 480
 cagcaaaacc ccttcagca gcccgagggt cgcggggggc ttgggcagag gggctcctca 540
 aggcaggggt ctccaggatc cgtatccaag cagaaacat gtgatttgcc tctgcgcctg 600
 ctggttccca cccaatttgt tggagccatc ataggaaaag aagggtgccac cattcggaac 660
 atcaccaaac agaccagtc taaaatcgat gtccaccgta aagaaaatgc gggggctgct 720
 gagaagtoga ttactatcct ctctactcct gaaggcacct ctgcggcttg taagtctatt 780
 ctggagatta tgcataagga agctcaagat ataaaattca cagaagagat ccccttgaag 840
 attttagctc ataataactt tggtggacgt cttattggta aagaaggag aaatcttaa 900
 aaaattgagc aagacacaga cactaaaatc acgatatctc cattgcagga attgacgctg 960

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168

180	185	190
Pro Cys Asp Leu Pro Leu Arg Leu Leu Val Pro Thr Gln Phe Val Gly		
195	200	205
Ala Ile Ile Gly Lys Glu Gly Ala Thr Ile Arg Asn Ile Thr Lys Gln		
210	215	220
Thr Gln Ser Lys Ile Asp Val His Arg Lys Glu Asn Ala Gly Ala Ala		
225	230	235 240
Glu Lys Ser Ile Thr Ile Leu Ser Thr Pro Glu Gly Thr Ser Ala Ala		
	245	250 255
Cys Lys Ser Ile Leu Glu Ile Met His Lys Glu Ala Gln Asp Ile Lys		
	260	265 270
Phe Thr Glu Glu Ile Pro Leu Lys Ile Leu Ala His Asn Asn Phe Val		
	275	280 285
Gly Arg Leu Ile Gly Lys Glu Gly Arg Asn Leu Lys Lys Ile Glu Gln		
	290	295 300
Asp Thr Asp Thr Lys Ile Thr Ile Ser Pro Leu Gln Glu Leu Thr Leu		
	305	310 315 320
Tyr Asn Pro Glu Arg Thr Ile Thr Val Lys Gly Asn Val Glu Thr Cys		
	325	330 335
Ala Lys Ala Glu Glu Glu Ile Met Lys Lys Ile Arg Glu Ser Tyr Glu		
	340	345 350
Asn Asp Ile Ala Ser Met Asn Leu Gln Ala His Leu Ile Pro Gly Leu		
	355	360 365
Asn Leu Asn Ala Leu Gly Leu Phe Pro Pro Thr Ser Gly Met Pro Pro		
	370	375 380
Pro Thr Ser Gly Pro Pro Ser Ala Met Thr Pro Pro Tyr Pro Gln Phe		
	385	390 395 400
Glu Gln Ser Glu Thr Glu Thr Val His Leu Phe Ile Pro Ala Leu Ser		
	405	410 415
Val Gly Ala Ile Ile Gly Lys Gln Gly Gln His Ile Lys Gln Leu Ser		
	420	425 430
Arg Phe Ala Gly Ala Ser Ile Lys Ile Ala Pro Ala Glu Ala Pro Asp		
	435	440 445
Ala Lys Val Arg Met Val Ile Ile Thr Gly Pro Pro Glu Ala Gln Phe		
	450	455 460
Lys Ala Gln Gly Arg Ile Tyr Gly Lys Ile Lys Glu Glu Asn Phe Val		
	465	470 475 480

Ser Pro Lys Glu Glu Val Lys Leu Glu Ala His Ile Arg Val Pro Ser
 485 490 495

Phe Ala Ala Gly Arg Val Ile Gly Lys Gly Gly Lys Thr Val Asn Glu
 500 505 510

Leu Gln Asn Leu Ser Ser Ala Glu Val Val Val Pro Arg Asp Gln Thr
 515 520 525

Pro Asp Glu Asn Asp Gln Val Val Val Lys Ile Thr Gly His Phe Tyr
 530 535 540

Ala Cys Gln Val Ala Gln Arg Lys Ile Gln Glu Ile Leu Thr Gln Val
 545 550 555 560

Lys Gln His Gln Gln Gln Lys Ala Leu Gln Ser Gly Pro Pro Gln Ser
 565 570 575

Arg Arg Lys

<210> 349

<211> 207

<212> DNA

<213> Homo sapiens

<400> 349

atgtggcagc cectcttctt caagtggctc ttgtcctggt gccctgggag ttctcaaatt 60
 gctgcagcag cctccacca gcctgaggat gacatcaata cacagaggaa gaagagtcag 120
 gaaaagatga gagaagttac agactctcct gggcgacccc gagagcttac cattcctcag 180
 acttcttcac atggtgctaa cagattt 207

<210> 350

<211> 69

<212> PRT

<213> Homo sapiens

<400> 350

Met Trp Gln Pro Leu Phe Phe Lys Trp Leu Leu Ser Cys Cys Pro Gly
 5 10 15

Ser Ser Gln Ile Ala Ala Ala Ala Ser Thr Gln Pro Glu Asp Asp Ile
 20 25 30

Asn Thr Gln Arg Lys Lys Ser Gln Glu Lys Met Arg Glu Val Thr Asp
 35 40 45

Ser Pro Gly Arg Pro Arg Glu Leu Thr Ile Pro Gln Thr Ser Ser His
 50 55 60

Gly Ala Asn Arg Phe
 65

